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- (71) Applicants (for all designated States except US): SAGAMI CHEMICAL RESEARCH CENTER [JP/JP]; 4-1, Nishi-Ohnuma 4-chome, Sagamihara-shi, Kanagawa 229-0012 (JP). PROTEGENE INC. [JP/JP]; 2-20-3, Naka-cho, Meguro-ku, Tokyo 153-0065 (JP).
- (72) Inventors; and
- (75) Inventors/Applicants (for US only): KATO, Seishi [JP/JP]; 3-46-50, Wakamatsu, Sagamihara-shi, Kanagawa 229-0014 (JP). KIMURA, Tomoko [JP/JP]; 715, 2-9-1, Kohoku, Tsuchiura-shi, Ibaraki 300-0032 (JP).

- (74) Agents: AOYAMA, Tamotsu et al.; Aoyama & Partners, IMP Building, 3-7, Shiromi 1-chome, Chuo-ku, Osaka-shi, Osaka 540-0001 (JP).
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DESCRIPTION

Human Proteins Having Hydrophobic

Domains and DNAs Encoding These Proteins

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#### TECHNICAL FIELD

The present invention relates to human proteins having hydrophobic domains, DNAs encoding these proteins, eukarvotic for these DNAs, vectors expressing these DNAs and antibodies directed to these proteins. The proteins of the present invention can be employed as pharmaceuticals or as antigens for preparing antibodies directed to these proteins. The human cDNAs of the present invention can be utilized as probes for genetic diagnosis and gene sources for gene therapy. Furthermore, the cDNAs can be utilized as gene sources for producing the proteins encoded by these cDNAs in large quantities. Cells into which these genes are introduced to express secretory proteins or membrane proteins in large quantities can be utilized for detection of the corresponding receptors or ligands, screening of novel small molecule pharmaceuticals and the like. The antibodies of the present invention can be utilized for the detection, quantification, purification and the like of the proteins of the present invention.

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#### BACKGROUND ART

Cells secrete many proteins extracellularly. These secretory proteins play important roles in the proliferation control, the differentiation induction, the transport, the biophylaxis, and the like of the cells. Unlike intracellular proteins, the secretory proteins exert their actions outside the cells. Therefore, they can be administered in the intracorporeal manner such as so that they possess injection or the drip, potentialities as pharmaceuticals. In fact, a number of human secretory proteins such as interferons, interleukins, erythropoietin, thrombolytic agents and the like currently employed as pharmaceuticals. In addition, secretory proteins other than those described above are undergoing clinical trials for developing their use pharmaceuticals. It is believed that the human cells produce many unknown secretory proteins. Availability of these secretory proteins as well as genes encoding them expected to lead to development of novel pharmaceuticals utilizing them.

On the other hand, membrane proteins play signal receptors, ion important roles, as channels, transporters and the like in the material transport and the signal transduction through the cell membrane. Examples thereof include receptors for various cytokines, ion

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channels for the sodium ion, the potassium ion, the chloride ion and the like, transporters for saccharides and amino acids and the like. The genes for many of them have already been cloned. It has been clarified that abnormalities in these membrane proteins are involved in a number of previously cryptogenic diseases. Therefore, discovery of a new membrane protein is expected to lead to elucidation of the causes of many diseases, so that isolation of new genes encoding the membrane proteins has been desired.

Heretofore, due to difficulty in the purification from human cells, many of these secretory proteins and membrane proteins have been isolated by genetic approaches. A general method is the so-called expression cloning method, in which a cDNA library is introduced into eukaryotic cells to express cDNAs, and the cells secreting, or expressing on the surface of membrane, the protein having the activity of interest are then screened. However, only genes for proteins with known functions can be cloned by using this method.

In general, a secretory protein or a membrane protein possesses at least one hydrophobic domain within the protein. After synthesis on ribosomes, such domain works as a secretory signal or remains in the phospholipid membrane to be entrapped in the membrane. Accordingly, if the existence of a highly hydrophobic domain is observed in the amino acid sequence of a protein encoded by a cDNA when the

whole base sequence of the full-length cDNA is determined, it is considered that the cDNA encodes a secretory protein or a membrane protein.

#### 5 OBJECTS OF INVENTION

The main object of the present invention is to provide novel human proteins having hydrophobic domains, DNAs encoding these proteins, expression vectors for these DNAs, transformed eukaryotic cells that are capable of expressing these DNAs and antibodies directed to these proteins. This object as well as other objects and advantages of the present invention will become apparent to those skilled in the art from the following description with reference to the accompanying drawings.

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#### SUMMARY OF INVENTION

As the result of intensive studies, the present inventors have successfully cloned cDNAs encoding proteins having hydrophobic domains from the human full-length cDNA bank, thereby completing the present invention. Thus, the present invention provides a human protein having hydrophobic domain(s), namely a protein comprising any one of an amino acid sequence selected from the group consisting of SEQ ID NOS: 1 to 10, 31 to 40, 61 to 70, 91 to 100 and 121 to 130. Moreover, the present invention provides a DNA

encoding said protein, exemplified by a cDNA comprising any one of a base sequence selected from the group consisting of SEQ ID NOS: 11 to 30, 41 to 60, 71 to 90, 101 to 120 and 131 to 150, an expression vector that is capable of expressing said DNA by in vitro translation or in eukaryotic cells, a transformed eukaryotic cell that is capable of expressing said DNA and of producing said protein and an antibody directed to said protein.

#### 10 BRIEF DESCRIPTION OF DRAWINGS

Fig. 1 illustrates the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP03171.

Fig. 2 illustrates the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP03424.

Fig. 3 illustrates the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP03444.

20 Fig. 4 illustrates the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP03478.

Fig. 5 illustrates the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP03499.

6 illustrates the Fig. hydrophobicity/hydrophilicity profile of the protein encoded by clone HP03500. Fig. 7 illustrates the 5 hydrophobicity/hydrophilicity profile of the protein encoded by clone HP10691. Fig. 8 illustrates the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP10703. 9 10 Fig. illustrates the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP10711. 10 Fig. illustrates the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP10712. 15 the Fig. 11 illustrates hydrophobicity/hydrophilicity profile of the protein encoded by clone HP03010. 12 illustrates the Fig. 20 hydrophobicity/hydrophilicity profile of the protein encoded by clone HP03576. Fig. 13 the illustrates hydrophobicity/hydrophilicity profile of the protein encoded by clone HP03611. 25 illustrates the Fig. 14

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hydrophobicity/hydrophilicity profile of the protein encoded by clone HP03612.

Fig. 15 illustrates the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP10407.

Fig. 16 illustrates the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP10713.

Fig. 17 illustrates the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP10714.

Fig. 18 illustrates the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP10716.

15 Fig. 19 illustrates the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP10717.

Fig. 20 illustrates the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP10718.

Fig. 21 illustrates the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP03745.

Fig. 22 illustrates the hydrophobicity/hydrophilicity profile of the protein encoded

by clone HP03747.

Fig. 23 illustrates the hydrophobicity/hydrophilicity profile of the protein encoded

by clone HP10719.

5 Fig. 24 illustrates the

hydrophobicity/hydrophilicity profile of the protein encoded by clone HP10720.

Fig. 25 illustrates the

hydrophobicity/hydrophilicity profile of the protein encoded by clone HP10721.

Fig. 26 illustrates the

hydrophobicity/hydrophilicity profile of the protein encoded by clone HP10725.

Fig. 27 illustrates the

hydrophobicity/hydrophilicity profile of the protein encoded by clone HP10727.

Fig. 28 illustrates the

hydrophobicity/hydrophilicity profile of the protein encoded by clone HP10728.

20 Fig. 29 illustrates the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP10730.

Fig. 30 illustrates the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP10742.

Fig.

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illustrates . Fig. 31 the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP03800. Fig. 32 illustrates the hydrophobicity/hydrophilicity profile of the protein encoded 5 by clone HP03831. Fig. 33 illustrates the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP03879. 10 Fig. 34 illustrates the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP03880. Fig. 35 illustrates the hydrophobicity/hydrophilicity profile of the protein encoded 15 by clone HP10704. Fig. 36 illustrates the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP10715. 37 illustrates the Fig. hydrophobicity/hydrophilicity profile of the protein encoded 20 by clone HP10724. 38 illustrates the Fig. hydrophobicity/hydrophilicity profile of the protein encoded by clone HP10733.

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illustrates

the

hydrophobicity/hydrophilicity profile of the protein encoded by clone HP10734.

Fig. 40 illustrates the

hydrophobicity/hydrophilicity profile of the protein encoded by clone HP10756.

Fig. 41 illustrates the

hydrophobicity/hydrophilicity profile of the protein encoded by clone HP03670.

Fig. 42 illustrates the

hydrophobicity/hydrophilicity profile of the protein encoded by clone HP03688.

Fig. 43 illustrates the

hydrophobicity/hydrophilicity profile of the protein encoded by clone HP03825

Fig. 44 illustrates the

hydrophobicity/hydrophilicity profile of the protein encoded by clone HP03877.

Fig. 45 illustrates the

hydrophobicity/hydrophilicity profile of the protein encoded 20 by clone HP10765.

Fig. 46 illustrates the

hydrophobicity/hydrophilicity profile of the protein encoded by clone HP10766.

Fig. 47 illustrates the

25 hydrophobicity/hydrophilicity profile of the protein encoded

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by clone HP10770.

Fig. 48 illustrates the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP10772.

Fig. 49 illustrates the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP10773.

Fig. 50 illustrates the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP10776.

#### DETAILED DESCRIPTION OF THE INVENTION

obtained, for example, by a method for isolating proteins from human organs, cell lines or the like, a method for preparing peptides by the chemical synthesis based on the amino acid sequences of the present invention, or a method for producing proteins by the recombinant DNA technology using the DNAs encoding the hydrophobic domains of the present invention. Among these, the method for producing proteins by the recombinant DNA technology is preferably employed. For example, the proteins can be expressed in vitro by preparing an RNA by in vitro transcription from a vector having the cDNA of the present invention, and then carrying out in vitro translation using this RNA as a

template. Alternatively, incorporation of the translated region into a suitable expression vector by the method known in the art may lead to expression of a large amount of the encoded protein in prokaryotic cells such as *Escherichia coli*, *Bacillus subtilis*, etc., and eukaryotic cells such as yeasts, insect cells, mammalian cells, etc.

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In the case where the protein of the present invention is produced by expressing the DNA by in vitro translation, the protein of the present invention can be produced in vitro by incorporating the translated region of this cDNA into a vector having an RNA polymerase promoter, and then adding the vector to an in vitro translation system such as a rabbit reticulocyte lysate or a wheat germ extract, which contains an RNA polymerase corresponding to the promoter. The RNA polymerase promoters are exemplified by T7, T3, SP6 and the like. The vectors containing promoters for these RNA polymerases are exemplified by pKA1, pCDM8, pT3/T7 18, pT7/3 19, pBluescript II and the like. Furthermore, the protein of the present invention can be expressed in the secreted form or the form incorporated in the microsome membrane when a canine pancreas microsome or the like is added to the reaction system.

In the case where the protein of the present invention is produced by expressing the DNA in a microorganism such as Escherichia coli etc., a recombinant

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expression vector in which the translated region of the cDNA of the present invention is incorporated into an expression vector having an origin which is capable of replicating in the microorganism, a promoter, a ribosome-binding site, a cDNA-cloning site, a terminator and the like is constructed. After transformation of the host cells with this expression vector, the resulting transformant is cultivated, whereby the protein encoded by the cDNA can be produced in large quantities in the microorganism. In this case, a protein fragment containing any translated region can be obtained by adding an initiation codon and a termination codon in front of and behind the selected translated region to express the protein. Alternatively, the protein can be expressed as a fusion protein with another protein. Only the portion of the protein encoded by the cDNA can be obtained by cleaving this fusion protein with a suitable protease. The expression vectors for Escherichia coli are exemplified by the pUC series, pBluescript II, the pET expression system, the pGEX expression system and the like.

In the case where the protein of the present invention is produced by expressing the DNA in eukaryotic cells, the protein of the present invention can be produced as a secretory protein, or as a membrane protein on the surface of cell membrane, by incorporating the translated region of the cDNA into an expression vector for eukaryotic

cells that has a promoter, a splicing region, a poly(A) addition site and the like, and then introducing the vector into the eukaryotic cells. The expression vectors are exemplified by pKA1, pED6dpc2, pCDM8, pSVK3, pMSG, pSVL, pBK-CMV, pBK-RSV, EBV vectors, pRS, pYES2 and the like. Examples of eukaryotic cells to be used in general include mammalian cultured cells such as monkey kidney COS7 cells, Chinese hamster ovary CHO cells and the like, budding yeasts, fission yeasts, silkworm cells, Xenopus oocytes and the like. Any eukaryotic cells may be used as long as they are capable of expressing the proteins of the present invention. The expression vector can be introduced into the eukaryotic cells by using a method known in the art such as the electroporation method, the Calcium phosphate method, the liposome method, the DEAE-dextran method and the like.

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After the protein of the present invention is expressed in prokaryotic cells or eukaryotic cells, the protein of interest can be isolated and purified from the culture by a combination of separation procedures known in the art. Examples of the separation procedures include treatment with a denaturing agent such as urea or detergent, sonication, enzymatic digestion, salting-out or solvent precipitation, dialysis, centrifugation, ultrafiltration, gel filtration, SDS-PAGE, isoelectric focusing, ion-exchange chromatography, hydrophobic

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chromatography, affinity chromatography, reverse phase chromatography and the like.

The proteins of the present invention also include peptide fragments (of 5 amino acid residues or more) containing any partial amino acid sequences in the amino acid sequences represented by SEQ ID NOS: 1 to 10, 31 to 40, 61 to 70, 91 to 100 and 121 to 130. These peptide fragments can be utilized as antigens for preparation of antibodies. Among the proteins of the present invention, those having the signal sequences are secreted in the form of mature proteins after the signal sequences are removed. Therefore, these mature proteins shall come within the scope of the protein of the present invention. The N-terminal amino acid sequences of the mature proteins can be easily determined by using the method for the determination of cleavage site of a signal sequence [JP-A 8-187100]. Furthermore, some membrane proteins undergo the processing on the cell surface to be converted to the secreted forms. Such proteins or peptides in the secreted forms shall also come within the scope of the protein of the present invention. In the case where sugar chain-binding sites are present in the amino acid sequences of the proteins, expression of the proteins in appropriate eukaryotic cells affords the proteins to which sugar chains are added. Accordingly, such proteins or peptides to which sugar chains are added shall also come

within the scope of the protein of the present invention.

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The DNAs of the present invention include all the DNAs encoding the above-mentioned proteins. These DNAs can be obtained by using a method for chemical synthesis, a method for cDNA cloning and the like.

The cDNAs of the present invention can be cloned, for example, from cDNA libraries derived from the human The cDNAs are synthesized by using poly(A) RNAs extracted from human cells as templates. The human cells may be cells delivered from the human body, for example, by the operation or may be the cultured cells. The cDNAs can be synthesized by using any method such as the Okayama-Berg method [Okayama, H. and Berg, P., Mol. Cell. Biol. 2: 161-170 (1982)], the Gubler-Hoffman method [Gubler, U. Hoffman, J., Gene 25: 263-269 (1983)] and the like. However, it is desirable to use the capping method [Kato, S. et al., Gene 150: 243-250 (1994)], as exemplified in Examples, in order to obtain a full-length clone in an effective manner. In addition, commercially available human cDNA libraries can be utilized. The cDNAs of the present invention can be cloned libraries by synthesizing from the CDNA oligonucleotide on the basis of base sequences of portion in the cDNA of the present invention and screening the cDNA libraries using this oligonucleotide as a probe for colony or plaque hybridization according to a method known in the art. In addition, the cDNA fragments of the present invention can be prepared from an mRNA isolated from human cells by the RT-PCR method in which oligonucleotides which hybridize with both termini of the cDNA fragment of interest are synthesized, which oligonucleotides are then used as the primers.

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present invention the are The cDNAs of characterized in that they comprise any one of the base sequences represented by SEQ ID NOS: 11 to 20, 41 to 50, 71 to 80, 101 to 110 and 131 to 140 or the base sequences represented by SEQ ID NOS: 21 to 30, 51 to 60, 81 to 90, 111 to 120 and 141 to 150. Tables 1 and 2 summarizes the clone number (HP number), the cell from which the cDNA clone was obtained, the total number of bases of the cDNA, and the number of the amino acid residues of the encoded protein, for each of the cDNAs.

Table 1

| Table | <u> </u> |           |              |                      |                       |                               |
|-------|----------|-----------|--------------|----------------------|-----------------------|-------------------------------|
| SEQ   | ID NO    | <b>).</b> | HP<br>number | Cell                 | Number<br>of<br>bases | Number of amino acid residues |
| 1,    | 11,      | 21        | HP03171      | Thymus               | 2042                  | 267                           |
| 2,    | 12,      |           | HP03424      | Liver                | 1433                  | 419                           |
| 3,    | 13,      |           | HP03444      | Kidney               | 1917                  | 415                           |
| 4,    | 14,      | 24        | HP03478      | Umbilical cord blood | 2258                  | 380                           |
| 5,    | 15,      | 25        | HP03499      | Kidney               | 1973                  | 585                           |
| 6,    | 16,      | 26        | HP03500      | kidney               | 1606                  | 331                           |
| 7,    | 17,      | 27        | HP10691      | Umbilical cord blood | 2380                  | 345                           |
| 8,    | 18,      | 28        | HP10703      | Kidney               | 2017                  | 89                            |
| 9,    | 19,      | 29        | HP10711      | Kidney               | 1606                  | 406                           |
| 10,   | 20,      | 30        | HP10712      | Kidney               | 1695                  | 192                           |
| 31,   | 41,      | 51        | HP03010      | Kidney               | 1551                  | 377                           |
| 32,   | 42,      | 52        | нР03576      | Kidney               | 1713                  | 81                            |
| 33,   | 43,      | 53        | HP03611      | Kidney               | 1758                  | 487                           |
| 34,   | 44,      | 54        | HP03612      | Kidney               | 1550                  | 375                           |
| 35,   | 45,      | 55        | HP10407      | Stomach cancer       | 1485                  | 350                           |
| 36,   | 46,      | 56        | HP10713      | Kidney               | 2694                  | 667                           |
| 37,   | 47,      | 57        | HP10714      | Umbilical cord blood | 3297                  | 464                           |
| 38,   | 48,      | 58        | HP10716      | Umbilical cord blood | 2126                  | 470                           |
| 39,   | 49,      | 59        | HP10717      | Kidney               | 1781                  | 243                           |
| 40,   | 50,      | 60        | HP10718      | Umbilical cord blood | 1788                  | 270                           |
| 61,   | 71,      | 81        | HP03745      | Kidney               | 1376                  | 389                           |
| 62,   | 72,      | 82        | HP03747      | Umbilical cord blood | 2392                  | 348                           |
| 63,   | 73,      | 83        | HP10719      | Kidney               | 1416                  | 261                           |
| 64,   | 74,      | 84        | HP10720      | Kidney               | 1347                  | 222                           |
| 65,   | 75,      | 85        | HP10721      | Kidney               | 2284                  | 183                           |

Table 2

| Table | -    |     |              | ·                    |                       |                               |
|-------|------|-----|--------------|----------------------|-----------------------|-------------------------------|
| SEQ   | ID 1 | 10  | HP<br>number | Cell                 | Number<br>of<br>bases | Number of amino acid residues |
| 66,   | 76,  | 86  | HP10725      | Kidney               | 1737                  |                               |
| 67,   | 77,  | 87  | HP10727      | Umbilical cord blood | 1556                  | 168                           |
| 68,   | 78,  | 88  | HP10728      | Umbilical cord blood | 1855                  | 243                           |
| 69,   | 79,  | 89  | HP10730      | Umbilical cord blood | 2530                  | 428                           |
| 70,   | 80,  | 90  | HP10742      | Umbilical cord blood | 1911                  | 283                           |
| 91,   | 101, | 111 | нр03800      | Umbilical cord blood | 1633                  | 476                           |
| 92,   | 102, | 112 | HP03831      | Kidney               | 1095                  | 226                           |
| 93,   | 103, | 113 | HP03879      | Kidney               | 1602                  | 305                           |
| 94,   | 104, | 114 | нр03880      | Kidney               | 897                   | 227                           |
| 95,   | 105, | 115 | HP10704      | Kidney               | 1866                  | 441                           |
| 96,   | 106, | 116 | . HP10715    | Umbilical cord blood | 2198                  | 265                           |
| 97,   | 107, | 117 | HP10724      | Umbilical cord blood | 2180                  | 208                           |
| 98,   | 108, | 118 | HP10733      | Umbilical cord blood | 1527                  | 400                           |
| 99,   | 109, | 119 | HP10734      | Umbilical cord blood | 1905                  | 192                           |
| 100,  | 110, | 120 | HP10756      | Kidney               | 998                   | 260                           |
| 121,  | 131, | 141 | HP03670      | Umbilical cord blood | 1622                  | 337                           |
| 122,  | 132, | 142 | HP03688      | Umbilical cord blood | 2475                  | 236                           |
| 123,  | 133, | 143 | HP03825      | Kidney               | 1739                  | 560                           |
| 124,  | 134, | 144 | HP03877      | Kidney               | 2005                  | 406                           |
| 125,  | 135, | 145 | HP10765      | Umbilical cord blood | 1558                  | 453                           |
| 126,  | 136, | 146 | HP10766      | Kidney               | 1005                  | 59                            |
| 127,  | 137, | 147 | HP10770      | Kidney               | 969                   | 210                           |
| 128,  | 138, | 148 | HP10772      | Kidney               | 1241                  | 165                           |
| 129,  | 139, | 149 | HP10773      | Kidney               | 1174                  | 162                           |
| 130,  | 140, | 150 | HP10776      | Kidney               | 1012                  | 221                           |

The same clones as the cDNAs of the present invention can be easily obtained by screening the cDNA libraries constructed from the human cell lines or human

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tissues utilized in the present invention using an oligonucleotide probe synthesized on the basis of the base sequence of the cDNA provided in any one of SEQ ID NOS: 11 to 30, 41 to 60, 71 to 90, 101 to 120 and 131 to 150.

In general, the polymorphism due to the individual differences is frequently observed in human genes. Accordingly, any cDNA in which one or plural nucleotides are added, deleted and/or substituted with other nucleotides in SEQ ID NOS: 11 to 30, 41 to 60, 71 to 90, 101 to 120 and 131 to 150 shall come within the scope of the present invention.

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Similarly, any protein in which one or plural amino acids are added, deleted and/or substituted with other amino acids resulting from the above-mentioned changes shall come within the scope of the present invention, as long as the protein possesses the activity of the protein having any one of the amino acid sequences represented by SEQ ID NOS: 1 to 10, 31 to 40, 61 to 70, 91 to 100 and 121 to 130.

The cDNAs of the present invention also include cDNA fragments (of 10 bp or more) containing any partial base sequence in the base sequences represented by SEQ ID NOS: 11 to 20, 41 to 50, 71 to 80, 101 to 110 and 131 to 140 or in the base sequences represented by SEQ ID NOS: 21 to 30, 51 to 60, 81 to 90, 111 to 120 and 141 to 150. Also, DNA fragments consisting of a sense strand and an anti-sense strand shall come within this scope. These DNA fragments can

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be utilized as the probes for the genetic diagnosis.

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The antibody of the present invention can be obtained from a serum after immunizing an animal using the protein of the present invention as an antigen. A peptide that is chemically synthesized based on the amino acid sequence of the present invention and a protein expressed in eukaryotic or prokaryotic cells can be used as an antigen. Alternatively, an antibody can be prepared by introducing the above-mentioned expression vector for eukaryotic cells into the muscle or the skin of an animal by injection or by using a gene gun and then collecting a serum therefrom (JP-A 7-313187). Animals that can be used include a mouse, a rat, a rabbit, a goat, a chicken and the like. A monoclonal antibody directed to the protein of the present invention can be produced by fusing B cells collected from the spleen of the immunized animal with myelomas to generate hybridomas.

In addition to the activities and uses described above, the polynucleotides and proteins of the present invention may exhibit one or more of the uses or biological activities (including those associated with assays cited herein) identified below. Uses or activities described for proteins of the present invention may be provided by administration or use of such proteins or by administration or use of polynucleotides encoding such proteins (such as, for example, in gene therapies or vectors suitable for

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introduction of DNA).

#### Research Uses and Utilities

polynucleotides provided by the The present invention can be used by the research community for various 5 The polynucleotides can be used purposes. to protein for recombinant analysis, characterization therapeutic use; as markers for tissues in which corresponding protein is preferentially expressed constitutively or at а particular stage of 10 differentiation or development or in disease states); as molecular weight markers on Southern gels; as chromosome markers or tags (when labeled) to identify chromosomes or to map related gene positions; to compare with endogenous DNA identify potential sequences in patients to 15 disorders; as probes to hybridize and thus discover novel, related DNA sequences; as a source of information to derive PCR primers for genetic fingerprinting; as a probe "subtract-out" known sequences in the process of discovering other novel polynucleotides; for selecting and making 20 oligomers for attachment to a "gene chip" or other support, including for examination of expression patterns; to raise anti-protein antibodies using DNA immunization techniques; and as an antigen to raise anti-DNA antibodies or elicit another immune response. Where the polynucleotide encodes a 25 protein which binds or potentially binds to another protein (such as, for example, in a receptor-ligand interaction), the polynucleotide can also be used in interaction trap assays (such as, for example, that described in Gyuris et al., Cell '75:791-803 (1993)) to identify polynucleotides encoding the other protein with which binding occurs or to identify inhibitors of the binding interaction.

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The proteins provided by the present invention can similarly be used in assay to determine biological activity, including in a panel of multiple proteins for highthroughput screening; to raise antibodies or to elicit another immune response; as a reagent (including the labeled reagent) in assays designed to quantitatively determine levels of the protein (or its receptor) in biological fluids; as markers for tissues in which the corresponding protein is preferentially expressed (either constitutively or at a particular stage of tissue differentiation or development or in a disease state); and, of course, to isolate correlative receptors or ligands. Where the protein binds or potentially binds to another protein (such as, for example, in a receptor-ligand interaction), the protein can be used to identify the other protein with which binding occurs or to identify inhibitors of the binding interaction. Proteins involved in these binding interactions can also be used to screen for peptide or small molecule inhibitors or agonists of the binding interaction.

Any or all of these research utilities are capable of being developed into reagent grade or kit format for commercialization as research products.

Methods for performing the uses listed above are well known to those skilled in the art. References disclosing such methods include without limitation "Molecular Cloning: A Laboratory Manual", 2d ed., Cold Spring Harbor Laboratory Press, Sambrook, J., E.F. Fritsch and T. Maniatis eds., 1989, and "Methods in Enzymology: Guide to Molecular Cloning Techniques", Academic Press, Berger, S.L. and A.R. Kimmel eds., 1987.

#### Nutritional Uses

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Polynucleotides and proteins of the present invention can also be used as nutritional sources or supplements. Such uses include without limitation use as a protein or amino acid supplement, use as a carbon source, use as a nitrogen source and use as a source of carbohydrate. In such cases the protein or polynucleotide of the invention can be added to the feed of a particular organism or can be administered as a separate solid or liquid preparation, such as in the form of powder, pills, solutions, suspensions or capsules. In the case of microorganisms, the protein or polynucleotide of the invention can be added to the medium in or on which the microorganism is cultured.

### Activity

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A protein of the present invention may exhibit cytokine, cell proliferation (either inducing or inhibiting) or cell differentiation (either inducing or inhibiting) activity or may induce production of other cytokines in certain cell populations. Many protein factors discovered to date, including all known cytokines, have exhibited activity in one or more factor dependent cell proliferation assays, and hence the assays serve as a convenient confirmation of cytokine activity. The activity of a protein of the present invention is evidenced by any one of a number of routine factor dependent cell proliferation assays for cell lines including, without limitation, 32D, DA2, DA1G, T10, B9, B9/11, BaF3, MC9/G, M+ (preB M+), 2E8, RB5, DA1, 123, T1165, HT2, CTLL2, TF-1, Mo7e and CMK.

The activity of a protein of the invention may, among other means, be measured by the following methods:

Assays for T-cell or thymocyte proliferation include without limitation those described in: Current Protocols in Immunology, Ed by J. E. Coligan, A.M. Kruisbeek, D.H. Margulies, E.M. Shevach, W Strober, Pub. Greene Publishing Associates and Wiley-Interscience (Chapter 3, In Vitro assays for Mouse Lymphocyte Function 3.1-3.19; Chapter 7, Immunologic studies in Humans); Takai et al., J. Immunol. 137:3494-3500, 1986; Bertagnolli et al., J. Immunol.

145:1706-1712, 1990; Bertagnolli et al., Cellular Immunology 133:327-341, 1991; Bertagnolli, et al., J. Immunol. 149:3778-3783, 1992; Bowman et al., J. Immunol. 152: 1756-1761, 1994.

- 5 for cytokine Assays production and/or proliferation of spleen cells, lymph node cells thymocytes include, without limitation, those described in: Polyclonal T cell stimulation, Kruisbeek, A.M. and Shevach, E.M. In Current Protocols in Immunology, J.E.e.a. Coligan 10 eds. Vol 1 pp. 3.12.1-3.12.14, John Wiley and Sons, Toronto. 1994; and Measurement of mouse and human Interferon γ, Schreiber, R.D. In Current Protocols in Immunology. J.E.e.a. Coligan eds. Vol 1 pp. 6.8.1-6.8.8, John Wiley and Sons, Toronto. 1994.
- Assays for proliferation and differentiation of hematopoietic and lymphopoietic cells include, without limitation, those described in: Measurement of Human and Murine Interleukin 2 and Interleukin 4, Bottomly, K., Davis, L.S. and Lipsky, P.E. In Current Protocols in Immunology.

  J.E.e.a. Coligan eds. Vol 1 pp. 6.3.1-6.3.12, John Wiley and Sons, Toronto. 1991; deVries et al., J. Exp. Med. 173:1205-1211, 1991; Moreau et al., Nature 336:690-692, 1988; Greenberger et al., Proc. Natl. Acad. Sci. U.S.A. 80:2931-2938, 1983; Measurement of mouse and human interleukin 6-Nordan, R. In Current Protocols in Immunology. J.E.e.a.

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Coligan eds. Vol 1 pp. 6.6.1-6.6.5, John Wiley and Sons, Toronto. 1991; Smith et al., Proc. Natl. Acad. Sci. U.S.A. 83:1857-1861, 1986; Measurement of human Interleukin 11 - Bennett, F., Giannotti, J., Clark, S.C. and Turner, K. J. In Current Protocols in Immunology. J.E.e.a. Coligan eds. Vol 1 pp. 6.15.1 John Wiley and Sons, Toronto. 1991; Measurement of mouse and human Interleukin 9 - Ciarletta, A., Giannotti, J., Clark, S.C. and Turner, K.J. In Current Protocols in Immunology. J.E.e.a. Coligan eds. Vol 1 pp. 6.13.1, John Wiley and Sons, Toronto. 1991.

Assays for T-cell clone responses to antigens (which will identify, among others, proteins that affect APC-T cell interactions as well as direct T-cell effects by measuring proliferation and cytokine production) include, without limitation, those described in: Current Protocols in Immunology, Ed by J. E. Coligan, A.M. Kruisbeek, D.H. Margulies, E.M. Shevach, W Strober, Pub. Greene Publishing Associates and Wiley-Interscience (Chapter 3, In Vitro assays for Mouse Lymphocyte Function; Chapter 6, Cytokines and their cellular receptors; Chapter 7, Immunologic studies in Humans); Weinberger et al., Proc. Natl. Acad. Sci. USA 77:6091-6095, 1980; Weinberger et al., Eur. J. Immun. 11:405-411, 1981; Takai et al., J. Immunol. 137:3494-3500, 1986; Takai et al., J. Immunol. 140:508-512, 1988.

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A protein of the present invention may also exhibit immune stimulating or immune suppressing activity, including without limitation the activities for which assays are described herein. A protein may be useful in the treatment of various immune deficiencies and disorders (including severe combined immunodeficiency (SCID)), e.g., in regulating (up or down) growth and proliferation of T and/or B lymphocytes, as well as effecting the cytolytic activity of NK cells and other cell populations. immune deficiencies may be genetic or be caused by viral (e.g., HIV) as well as bacterial or fungal infections, or may result from autoimmune disorders. More specifically, infectious diseases causes by viral, bacterial, fungal or other infection may be treatable using a protein of the present invention, including infections by HIV, hepatitis viruses, herpesviruses, mycobacteria, Leishmania malaria spp. and various fungal infections candidiasis. Of course, in this regard, a protein of the present invention may also be useful where a boost to the immune system generally may be desirable, i.e., in the treatment of cancer.

Autoimmune disorders which may be treated using a protein of the present invention include, for example, connective tissue disease, multiple sclerosis, systemic lupus erythematosus, rheumatoid arthritis, autoimmune

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pulmonary inflammation, Guillain-Barre syndrome, autoimmune thyroiditis, insulin dependent diabetes mellitis, myasthenia graft-versus-host disease and autoimmune gravis, inflammatory eye disease. Such a protein of the present invention may also to be useful in the treatment of allergic reactions and conditions, such as asthma (particularly allergic asthma) or other respiratory problems. suppression is desired which immune conditions, in (including, for example, organ transplantation), may also be treatable using a protein of the present invention.

Using the proteins of the invention it may also be possible to immune responses, in a number of ways. Down regulation may be in the form of inhibiting or blocking an may in progress or response already The preventing the induction of an immune response. may be inhibited functions of activated T cells suppressing T cell responses or by inducing specific tolerance in T cells, or both. Immunosuppression of T cell responses is generally an active, non-antigen-specific, process which requires continuous exposure of the T cells to the suppressive agent. Tolerance, which involves inducing non-responsiveness or anergy in T cells, is distinguishable from immunosuppression in that it is generally antigenspecific and persists after exposure to the tolerizing agent has ceased. Operationally, tolerance can be demonstrated by WO 01/12660

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the lack of a T cell response upon reexposure to specific antigen in the absence of the tolerizing agent.

Down regulating or preventing one or more antigen functions (including without limitation B lymphocyte antigen functions (such as , for example, B7)), e.g., preventing high level lymphokine synthesis by activated T cells, will situations useful in of tissue, skin and organ transplantation and in graft-versus-host disease (GVHD). For example, blockage of T cell function should result in reduced tissue destruction in tissue transplantation. Typically, in tissue transplants, rejection the transplant is initiated through its recognition as foreign by T cells, followed by an immune reaction that destroys the transplant. The administration of a molecule which inhibits or blocks interaction of a B7 lymphocyte antigen with its natural ligand(s) on immune cells (such as a soluble, monomeric form of a peptide having B7-2 activity alone or in conjunction with a monomeric form of a peptide having an activity of another B lymphocyte antigen (e.g., B7-1, B7-3) or blocking antibody), prior to transplantation can lead to the binding of the molecule to the natural ligand(s) on the immune cells without transmitting the corresponding costimulatory signal. Blocking B lymphocyte antigen function in this matter prevents cytokine synthesis by immune cells, such as T cells, and thus acts as an immunosuppressant.

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Moreover, the lack of costimulation may also be sufficient to anergize the T cells, thereby inducing tolerance in a subject. Induction of long-term tolerance by B lymphocyte antigen-blocking reagents may avoid the necessity of repeated administration of these blocking reagents. To achieve sufficient immunosuppression or tolerance in a subject, it may also be necessary to block the function of a combination of B lymphocyte antigens.

The efficacy of particular blocking reagents in preventing organ transplant rejection or GVHD can be assessed using animal models that are predictive of efficacy in humans. Examples of appropriate systems which can be used include allogeneic cardiac grafts in rats and xenogeneic pancreatic islet cell grafts in mice, both of which have been used to examine the immunosuppressive effects of CTLA4Ig fusion proteins in vivo as described in Lenschow et al., Science 257:789-792 (1992) and Turka et al., Proc. Natl. Acad. Sci USA, 89:11102-11105 (1992). In addition, murine models of GVHD (see Paul ed., Fundamental Immunology, Raven Press, New York, 1989, pp. 846-847) can be used to determine the effect of blocking B lymphocyte antigen function in vivo on the development of that disease.

Blocking antigen function may also be therapeutically useful for treating autoimmune diseases.

Many autoimmune disorders are the result of inappropriate

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activation of T cells that are reactive against self tissue which promote and the production of cytokines and autoantibodies involved in the pathology of the diseases. Preventing the activation of autoreactive T cells may reduce or eliminate disease symptoms. Administration of reagents block costimulation of Т cells by disrupting receptor: ligand interactions of B lymphocyte antigens can be used to inhibit T cell activation and prevent production of autoantibodies or T cell-derived cytokines which may be involved in the disease process. Additionally, blocking induce reagents may antigen-specific tolerance autoreactive T cells which could lead to long-term relief from the disease. The efficacy of blocking reagents alleviating autoimmune disorders can preventing or determined using a number of well-characterized animal models of human autoimmune diseases. Examples include murine experimental autoimmune encephalitis, systemic erythmatosis in MRL/lpr/lpr mice or NZB hybrid mice, murine autoimmune collagen arthritis, diabetes mellitus in NOD mice and BB rats, and murine experimental myasthenia gravis (see Paul ed., Fundamental Immunology, Raven Press, New York, 1989, pp. 840-856).

Upregulation of an antigen function (preferably a B lymphocyte antigen function), as a means of up regulating immune responses, may also be useful in therapy.

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Upregulation of immune responses may be in the form of enhancing an existing immune response or eliciting an initial immune response. For example, enhancing an immune response through stimulating B lymphocyte antigen function may be useful in cases of viral infection. In addition, systemic viral diseases such as influenza, the common cold, and encephalitis might be alleviated by the administration of stimulatory forms of B lymphocyte antigens systemically.

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Alternatively, anti-viral immune responses may be enhanced in an infected patient by removing T cells from the patient, costimulating the T cells in vitro with viral antigen-pulsed APCs either expressing a peptide of the present invention or together with a stimulatory form of a soluble peptide of the present invention and reintroducing the in vitro activated T cells into the patient. Another method of enhancing anti-viral immune responses would be to isolate infected cells from a patient, transfect them with a nucleic acid encoding a protein of the present invention as described herein such that the cells express all or a portion of the protein on their surface, and reintroduce the transfected cells into the patient. The infected cells would now be capable of delivering a costimulatory signal to, and thereby activate, T cells in vivo.

In another application, up regulation or enhancement of antigen function (preferably B lymphocyte

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antigen function) may be useful in the induction of tumor immunity. Tumor cells (e.g., sarcoma, melanoma, lymphoma, leukemia, neuroblastoma, carcinoma) transfected with nucleic acid encoding at least one peptide of the present invention can be administered to a subject to overcome tumor-specific tolerance in the subject. If desired, the tumor cell can be transfected to express a combination of peptides. For example, tumor cells obtained from a patient can be transfected ex vivo with an expression vector directing the expression of a peptide having B7-2-like activity alone, or in conjunction with a peptide having B7-1-like activity and/or B7-3-like activity. The transfected tumor cells are returned to the patient to result in expression of the peptides on the surface of the transfected cell. Alternatively, gene therapy techniques can be used to target a tumor cell for transfection in vivo.

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The presence of the peptide of the present invention having the activity of a B lymphocyte antigen(s) on the surface of the tumor cell provides the necessary costimulation signal to T cells to induce a T cell mediated immune response against the transfected tumor cells. In addition, tumor cells which lack MHC class I or MHC class II molecules, or which fail to reexpress sufficient amounts of MHC class I or MHC class II molecules, can be transfected with nucleic acid encoding all or a portion of (e.g., a

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cytoplasmic-domain truncated portion) of an MHC class I lphachain protein and  $\beta$ , microglobulin protein or an MHC class II  $\alpha$  chain protein and an MHC class II  $\beta$  chain protein to thereby express MHC class I or MHC class II proteins on the cell surface. Expression of the appropriate class I or class II MHC in conjunction with a peptide having the activity of a B lymphocyte antigen (e.g., B7-1, B7-2, B7-3) induces a T cell mediated immune response against the transfected tumor cell. Optionally, a gene encoding an antisense construct which blocks expression of an MHC class II associated the invariant chain, can also protein, such as cotransfected with a DNA encoding a peptide having the activity of a B lymphocyte antigen to promote presentation of tumor associated antigens and induce tumor specific immunity. Thus, the induction of a T cell mediated immune response in a human subject may be sufficient to overcome tumor-specific tolerance in the subject.

The activity of a protein of the invention may, among other means, be measured by the following methods:

Suitable assays for thymocyte or splenocyte cytotoxicity include, without limitation, those described in: Current Protocols in Immunology, Ed by J. E. Coligan, A.M. Kruisbeek, D.H. Margulies, E.M. Shevach, W Strober, Pub. Greene Publishing Associates and Wiley-Interscience (Chapter 3, In Vitro assays for Mouse Lymphocyte Function 3.1-3.19;

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Chapter 7, Immunologic studies in Humans); Herrmann et al., Proc. Natl. Acad. Sci. USA 78:2488-2492, 1981; Herrmann et al., J. Immunol. 128:1968-1974, 1982; Handa et al., J. Immunol. 135:1564-1572, 1985; Takai et al., J. Immunol. 137:3494-3500, 1986; Takai et al., J. Immunol. 140:508-512, 1988; Herrmann et al., Proc. Natl. Acad. Sci. USA 78:2488-2492, 1981; Herrmann et al., J. Immunol. 128:1968-1974, 1982; Handa et al., J. Immunol. 135:1564-1572, 1985; Takai et al., J. Immunol. 137:3494-3500, 1986; Bowmanet al., J. Virology 61:1992-1998; Takai et al., J. Immunol. 140:508-512, 1988; Bertagnolli et al., Cellular Immunology 133:327-341, 1991; Brown et al., J. Immunol. 153:3079-3092, 1994.

Assays for T-cell-dependent immunoglobulin responses and isotype switching (which will identify, among others, proteins that modulate T-cell dependent antibody responses and that affect Th1/Th2 profiles) include, without limitation, those described in: Maliszewski, J. Immunol. 144:3028-3033, 1990; and Assays for B cell function: In vitro antibody production, Mond, J.J. and Brunswick, M. In Current Protocols in Immunology. J.E.e.a. Coligan eds. Vol 1 pp. 3.8.1-3.8.16, John Wiley and Sons, Toronto. 1994.

Mixed lymphocyte reaction (MLR) assays (which will identify, among others, proteins that generate predominantly Thl and CTL responses) include, without limitation, those described in: Current Protocols in Immunology, Ed by J. E.

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Coligan, A.M. Kruisbeek, D.H. Margulies, E.M. Shevach, W Strober, Pub. Greene Publishing Associates and Wiley-Interscience (Chapter 3, In Vitro assays for Mouse Lymphocyte Function 3.1-3.19; Chapter 7, Immunologic studies in Humans); Takai et al., J. Immunol. 137:3494-3500, 1986; Takai et al., J. Immunol. 140:508-512, 1988; Bertagnolli et al., J. Immunol. 149:3778-3783, 1992.

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Dendritic cell-dependent assays (which will identify, among others, proteins expressed by dendritic cells that activate naive T-cells) include, without 10 limitation, those described in: Guery et al., J. Immunol. 134:536-544, 1995; Inaba et al., Journal of Experimental Medicine 173:549-559, 1991; Macatonia et al., Journal of Immunology 154:5071-5079, 1995; Porgador et al., Journal of Experimental Medicine 182:255-260, 1995; Nair et al., 15 Journal of Virology 67:4062-4069, 1993; Huang et al., Science 264:961-965, 1994; Macatonia et al., Journal of Experimental Medicine 169:1255-1264, 1989; Bhardwaj et al., Journal of Clinical Investigation 94:797-807, 1994; and Inaba et al., Journal of Experimental Medicine 172:631-640, 20 1990.

Assays for lymphocyte survival/apoptosis (which will identify, among others, proteins that prevent apoptosis after superantigen induction and proteins that regulate lymphocyte homeostasis) include, without limitation, those

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described in: Darzynkiewicz et al., Cytometry 13:795-808, 1992; Gorczyca et al., Leukemia 7:659-670, 1993; Gorczyca et al., Cancer Research 53:1945-1951, 1993; Itoh et al., Cell 66:233-243, 1991; Zacharchuk, Journal of Immunology 145:4037-4045, 1990; Zamai et al., Cytometry 14:891-897, 1993; Gorczyca et al., International Journal of Oncology 1:639-648, 1992.

Assays for proteins that influence early steps of T-cell commitment and development include, without limitation, those described in: Antica et al., Blood 84:111-117, 1994; Fine et al., Cellular Immunology 155:111-122, 1994; Galy et al., Blood 85:2770-2778, 1995; Toki et al., Proc. Nat. Acad Sci. USA 88:7548-7551, 1991.

### Hematopoiesis Regulating Activity

15 A protein of the present invention may be useful in regulation of hematopoiesis and, consequently, in the treatment of myeloid or lymphoid cell deficiencies. Even marginal biological activity in support of colony forming cells or of factor-dependent cell lines 20 involvement in regulating hematopoiesis, e.g. in supporting the growth and proliferation of erythroid progenitor cells in combination with other cytokines, thereby alone or indicating utility, for example, in treating various anemias or for use in conjunction with irradiation/chemotherapy to 25 stimulate the production of erythroid precursors and/or

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erythroid cells; in supporting the growth and proliferation such of myeloid cells as granulocytes and monocytes/macrophages (i.e., traditional CSF activity) useful, for example, in conjunction with chemotherapy to prevent or treat consequent myelo-suppression; in supporting proliferation of megakaryocytes growth and consequently of platelets thereby allowing prevention or treatment of various platelet disorders such as thrombocytopenia, and generally for use in place of or complementary to platelet transfusions; and/or in supporting the growth and proliferation of hematopoietic stem cells which are capable of maturing to any and all of the abovementioned hematopoietic cells and therefore find therapeutic utility in various stem cell disorders (such as those usually treated with transplantation, including, without limitation, aplastic anemia and paroxysmal nocturnal hemoglobinuria), as well as in repopulating the stem cell compartment post irradiation/chemotherapy, either in-vivo or conjunction ex-vivo (i.e., in with bone marrow transplantation with peripheral progenitor cell or transplantation (homologous or heterologous)) as cells or genetically manipulated for gene therapy.

The activity of a protein of the invention may, among other means, be measured by the following methods:

25 Suitable assays for proliferation and

differentiation of various hematopoietic lines are cited above.

Assays for embryonic stem cell differentiation (which will identify, among others, proteins that influence embryonic differentiation hematopoiesis) include, without limitation, those described in: Johansson et al. Cellular Biology 15:141-151, 1995; Keller et al., Molecular and Cellular Biology 13:473-486, 1993; McClanahan et al., Blood 81:2903-2915, 1993.

10 Assays for stem cell survival and differentiation (which will identify, among others, proteins that regulate lympho-hematopoiesis) include, without limitation, those Methylcellulose colony forming assays, described in: Freshney, M.G. In Culture of Hematopoietic Cells. R.I. 15 Freshney, et al. eds. Vol pp. 265-268, Wiley-Liss, Inc., New York, NY. 1994; Hirayama et al., Proc. Natl. Acad. Sci. USA 89:5907-5911, 1992; Primitive hematopoietic colony forming cells with high proliferative potential, McNiece, I.K. and Briddell, R.A. In Culture of Hematopoietic Cells. R.I. 20 Freshney, et al. eds. Vol pp. 23-39, Wiley-Liss, Inc., New York, NY. 1994; Neben et al., Experimental Hematology 22:353-359, 1994; Cobblestone area forming cell assay, Ploemacher, R.E. In Culture of Hematopoietic Cells. R.I. Freshney, et al. eds. Vol pp. 1-21, Wiley-Liss, Inc., New 25 York, NY. 1994; Long term bone marrow cultures in the WO 01/12660 PCT/JP00/05356

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presence of stromal cells, Spooncer, E., Dexter, M. and Allen, T. In Culture of Hematopoietic Cells. R.I. Freshney, et al. eds. Vol pp. 163-179, Wiley-Liss, Inc., New York, NY. 1994; Long term culture initiating cell assay, Sutherland, H.J. In Culture of Hematopoietic Cells. R.I. Freshney, et al. eds. Vol pp. 139-162, Wiley-Liss, Inc., New York, NY. 1994.

### Tissue Growth Activity

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A protein of the present invention also may have utility in compositions used for bone, cartilage, tendon, ligament and/or nerve tissue growth or regeneration, as well as for wound healing and tissue repair and replacement, and in the treatment of burns, incisions and ulcers.

A protein of the present invention, which induces cartilage and/or bone growth in circumstances where bone is not normally formed, has application in the healing of bone fractures and cartilage damage or defects in humans and other animals. Such a preparation employing a protein of the invention may have prophylactic use in closed as well as open fracture reduction and also in the improved fixation of artificial joints. De novo bone formation induced by an osteogenic agent contributes to the repair of congenital, trauma induced, or oncologic resection induced craniofacial defects, and also is useful in cosmetic plastic surgery.

A protein of this invention may also be used in the treatment of periodontal disease, and in other tooth

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repair processes. Such agents may provide an environment to attract bone-forming cells, stimulate growth of bone-forming cells or induce differentiation of progenitors of bone-forming cells. A protein of the invention may also be useful in the treatment of osteoporosis or osteoarthritis, such as through stimulation of bone and/or cartilage repair or by blocking inflammation or processes of tissue destruction (collagenase activity, osteoclast activity, etc.) mediated by inflammatory processes.

Another category of tissue regeneration activity that may be attributable to the protein of the present invention is tendon/ligament formation. A protein of the present invention, which induces tendon/ligament-like tissue or other tissue formation in circumstances where such tissue is not normally formed, has application in the healing of tendon or ligament tears, deformities and other tendon or ligament defects in humans and other animals. Such preparation employing a tendon/ligament-like tissue inducing protein may have prophylactic use in preventing damage to tendon or ligament tissue, as well as use in the improved fixation of tendon or ligament to bone or other tissues, and in repairing defects to tendon or ligament tissue. De novo tendon/ligament-like tissue formation induced by composition of the present invention contributes to the repair of congenital, trauma induced, or other tendon or

ligament defects of other origin, and is also useful in cosmetic plastic surgery for attachment or repair of tendons or ligaments. The compositions of the present invention may provide an environment to attract tendon or ligament-forming cells, stimulate growth of tendon- or ligament-forming cells, differentiation of progenitors of induce ligament-forming cells, or induce growth of tendon/ligament cells or progenitors ex vivo for return in vivo to effect tissue repair. The compositions of the invention may also be in the treatment of tendinitis, carpal useful tendon or ligament defects. The and other syndrome compositions may also include an appropriate matrix and/or sequestering agent as a carrier as is well known in the art.

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The protein of the present invention may also be proliferation of neural cells useful for regeneration of nerve and brain tissue, i.e. for the treatment of central and peripheral nervous system diseases and neuropathies, as well as mechanical and traumatic disorders, which involve degeneration, death or trauma to neural cells or nerve tissue. More specifically, a protein 20 may be used in the treatment of diseases of the peripheral nerve injuries, such as peripheral nervous system, localized neuropathies, neuropathy and peripheral nervous system diseases, such as Alzheimer's, central Parkinson's disease, Huntington's disease, amyotrophic 25

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lateral sclerosis, and Shy-Drager syndrome. conditions which may be treated in accordance with the present invention include mechanical and traumatic disorders, such as spinal cord disorders, head trauma and cerebrovascular diseases such as stroke. Peripheral neuropathies resulting from chemotherapy or other medical therapies may also be treatable using a protein of the invention.

Proteins of the invention may also be useful to

10 promote better or faster closure of non-healing wounds,
including without limitation pressure ulcers, ulcers
associated with vascular insufficiency, surgical and
traumatic wounds and the like.

It is expected that a protein of the present invention may also exhibit activity for generation or regeneration of other tissues, such as organs (including, for example, pancreas, liver, intestine, kidney, skin, endothelium), muscle (smooth, skeletal or cardiac) and vascular (including vascular endothelium) tissue, or for promoting the growth of cells comprising such tissues. Part of the desired effects may be by inhibition or modulation of fibrotic scarring to allow normal tissue to regenerate. A protein of the invention may also exhibit angiogenic activity.

A protein of the present invention may also be

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useful for gut protection or regeneration and treatment of lung or liver fibrosis, reperfusion injury in various tissues, and conditions resulting from systemic cytokine damage.

A protein of the present invention may also be useful for promoting or inhibiting differentiation of tissues described above from precursor tissues or cells; or for inhibiting the growth of tissues described above.

The activity of a protein of the invention may, among other means, be measured by the following methods:

Assays for tissue generation activity include, without limitation, those described in: International Patent Publication No. W095/16035 (bone, cartilage, tendon); International Patent Publication No. W095/05846 (nerve, neuronal); International Patent Publication No. W091/07491 (skin, endothelium).

Assays for wound healing activity include, without limitation, those described in: Winter, Epidermal Wound Healing, pps. 71-112 (Maibach, HI and Rovee, DT, eds.), Year Book Medical Publishers, Inc., Chicago, as modified by Eaglstein and Mertz, J. Invest. Dermatol 71:382-84 (1978).

# Activin/Inhibin Activity

A protein of the present invention may also exhibit activin- or inhibin-related activities. Inhibins are characterized by their ability to inhibit the release of

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follicle stimulating hormone (FSH), while activins and are characterized by their ability to stimulate the release of follicle stimulating hormone (FSH). Thus, a protein of the present invention, alone or in heterodimers with a member of the inhibin  $\alpha$  family, may be useful as a contraceptive based on the ability of inhibins to decrease fertility in female mammals and decrease spermatogenesis in male mammals. Administration of sufficient amounts of other inhibins can induce infertility in these mammals. Alternatively, the protein of the invention, as a homodimer or as a heterodimer with other protein subunits of the inhibin- $\beta$  group, may be useful as a fertility inducing therapeutic, based upon the ability of activin molecules in stimulating FSH release from cells of the anterior pituitary. See, for example, United States Patent 4,798,885. A protein of the invention may also be useful for advancement of the onset of fertility in sexually immature mammals, so as to increase the lifetime reproductive performance of domestic animals such as cows, sheep and pigs.

The activity of a protein of the invention may, among other means, be measured by the following methods:

Assays for activin/inhibin activity include, without limitation, those described in: Vale et al., Endocrinology 91:562-572, 1972; Ling et al., Nature 321:779-782, 1986; Vale et al., Nature 321:776-779, 1986; Mason et

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al., Nature 318:659-663, 1985; Forage et al., Proc. Natl. Acad. Sci. USA 83:3091-3095, 1986.

# Chemotactic/Chemokinetic Activity

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A protein of the present invention may have chemotactic or chemokinetic activity (e.g., act as a chemokine) for mammalian cells, including, for example, monocytes, fibroblasts, neutrophils, T-cells, mast cells, endothelial cells. and/or epithelial eosinophils, Chemotactic and chemokinetic proteins can be used to mobilize or attract a desired cell population to a desired site of action. Chemotactic or chemokinetic proteins provide particular advantages in treatment of wounds and other trauma to tissues, as well as in treatment of localized lymphocytes, infections. For example, attraction of monocytes or neutrophils to tumors or sites of infection may result in improved immune responses against the tumor or infecting agent.

A protein or peptide has chemotactic activity for a particular cell population if it can stimulate, directly or indirectly, the directed orientation or movement of such cell population. Preferably, the protein or peptide has the ability to directly stimulate directed movement of cells. Whether a particular protein has chemotactic activity for a population of cells can be readily determined by employing such protein or peptide in any known assay for cell

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chemotaxis.

The activity of a protein of the invention may, among other means, be measured by the following methods:

Assays for chemotactic activity (which identify proteins that induce or prevent chemotaxis) consist of assays that measure the ability of a protein to induce the migration of cells across a membrane as well as the ability of a protein to induce the adhesion of one cell population to another cell population. Suitable assays for movement and adhesion include, without limitation, those described in: Current Protocols in Immunology, Ed by J.E. Coligan, A.M. Kruisbeek, D.H. Margulies, E.M. Shevach, W.Strober, Pub. Greene Publishing Associates and Wiley-Interscience (Chapter 6.12, Measurement of alpha and beta Chemokines 6.12.1-6.12.28; Taub et al. J. Clin. Invest. 95:1370-1376, 1995; Lind et al. APMIS 103:140-146, 1995; Muller et al Eur. J. Immunol. 25: 1744-1748; Gruber et al. J. Immunol. 152:5860-5867, 1994; Johnston et al. J. of Immunol. 153: 1762-1768, 1994.

## 20 <u>Hemostatic and Thrombolytic Activity</u>

A protein of the invention may also exhibit hemostatic or thrombolytic activity. As a result, such a protein is expected to be useful in treatment of various coagulation disorders (including hereditary disorders, such as hemophilias) or to enhance coagulation and other

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hemostatic events in treating wounds resulting from trauma, surgery or other causes. A protein of the invention may also be useful for dissolving or inhibiting formation of thromboses and for treatment and prevention of conditions resulting therefrom (such as, for example, infarction of cardiac and central nervous system vessels (e.g., stroke)).

The activity of a protein of the invention may, among other means, be measured by the following methods:

Assay for hemostatic and thrombolytic activity include, without limitation, those described in: Linet et al., J. Clin. Pharmacol. 26:131-140, 1986; Burdick et al., Thrombosis Res. 45:413-419, 1987; Humphrey et al., Fibrinolysis 5:71-79 (1991); Schaub, Prostaglandins 35:467-474, 1988.

## Receptor/Ligand Activity

A protein of the present invention may also demonstrate activity as receptors, receptor ligands or inhibitors or agonists of receptor/ligand interactions. Examples of such receptors and ligands include, without limitation, cytokine receptors and their ligands, receptor kinases and their ligands, receptor phosphatases and their ligands, receptors involved in cell-cell interactions and their ligands (including without limitation, cellular adhesion molecules (such as selectins, integrins and their ligands) and receptor/ligand pairs involved in antigen

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presentation, antigen recognition and development of cellular and humoral immune responses). Receptors and ligands are also useful for screening of potential peptide or small molecule inhibitors of the relevant receptor/ligand interaction. A protein of the present invention (including, without limitation, fragments of receptors and ligands) may themselves be useful as inhibitors of receptor/ligand interactions.

The activity of a protein of the invention may, among other means, be measured by the following methods:

Suitable assays for receptor-ligand activity include without limitation those described in: Current Protocols in Immunology, Ed by J.E. Coligan, A.M. Kruisbeek, D.H. Margulies, E.M. Shevach, W.Strober, Pub. Greene Publishing Associates and Wiley-Interscience (Chapter 7.28, Measurement of Cellular Adhesion under static conditions 7.28.1-7.28.22), Takai et al., Proc. Natl. Acad. Sci. USA 84:6864-6868, 1987; Bierer et al., J. Exp. Med. 168:1145-1156, 1988; Rosenstein et al., J. Exp. Med. 169:149-160 1989; Stoltenborg et al., J. Immunol. Methods 175:59-68, 1994; Stitt et al., Cell 80:661-670, 1995.

## Anti-Inflammatory Activity

Proteins of the present invention may also exhibit anti-inflammatory activity. The anti-inflammatory activity

may be achieved by providing a stimulus to cells involved in the inflammatory response, by inhibiting or promoting cellcell interactions (such as, for example, cell adhesion), by inhibiting or promoting chemotaxis of cells involved in the promoting inflammatory process, inhibiting or extravasation, or by stimulating or suppressing production of other factors which more directly inhibit or promote an inflammatory response. Proteins exhibiting such activities can be used to treat inflammatory conditions including chronic or acute conditions), including without limitation inflammation associated with infection (such as septic shock, sepsis or systemic inflammatory response syndrome (SIRS)), ischemia-reperfusion injury, endotoxin lethality, arthritis, complement-mediated hyperacute rejection, nephritis, cytokine or chemokine-induced lung injury, inflammatory bowel disease, Crohn's disease or resulting from over production of cytokines such as TNF or IL-1. Proteins of the invention may also be useful to treat anaphylaxis and hypersensitivity to an antigenic substance or material.

# Tumor Inhibition Activity

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In addition to the activities described above for immunological treatment or prevention of tumors, a protein of the invention may exhibit other anti-tumor activities. A protein may inhibit tumor growth directly or indirectly

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(such as, for example, via ADCC). A protein may exhibit its tumor inhibitory activity by acting on tumor tissue or tumor precursor tissue, by inhibiting formation of tissues necessary to support tumor growth (such as, for example, by inhibiting angiogenesis), by causing production of other factors, agents or cell types which inhibit tumor growth, or by suppressing, eliminating or inhibiting factors, agents or cell types which promote tumor growth.

### Other Activities

A protein of the invention may also exhibit one or more of the following additional activities or effects: inhibiting the growth, infection or function of, or killing, infectious agents, including, without limitation, bacteria, viruses, funqi and other parasites; effecting (suppressing or enhancing) bodily characteristics, including, without limitation, height, weight, hair color, eye color, skin, fat to lean ratio or other tissue pigmentation, or organ or body part size or shape (such as, for example, augmentation or diminution, change in bone form or shape); effecting biorhythms or cardiac cycles or rhythms; effecting the fertility of male or female subjects; effecting the metabolism, catabolism, anabolism, processing, utilization, storage or elimination of dietary fat, lipid, protein, carbohydrate, vitamins, minerals, cofactors or

nutritional factors or component(s); effecting behavioral characteristics, including, without limitation, appetite, libido, stress, cognition (including cognitive disorders), depression (including depressive disorders) and violent behaviors; providing analgesic effects or other pain reducing effects; promoting differentiation and growth of embryonic stem cells in lineages other than hematopoietic lineages; hormonal or endocrine activity; in the case of enzymes, correcting deficiencies of the enzyme and treating deficiency-related diseases; treatment of hyperproliferative disorders (such as, for example, psoriasis); immunoglobulinlike activity (such as, for example, the ability to bind antigens or complement); and the ability to act as an antigen in a vaccine composition to raise an immune response against such protein or another material or entity which is cross-reactive with such protein.

### Examples

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in more detail by the following Examples, but Examples are not intended to restrict the present invention. The basic procedures with regard to the recombinant DNA and the enzymatic reactions were carried out according to the literature ["Molecular Cloning. A Laboratory Manual", Cold

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Spring Harbor Laboratory, 1989]. Unless otherwise stated. restriction enzymes and various modifying enzymes to be used were those available from Takara Shuzo. The buffer compositions and the reaction conditions for each of the enzyme reactions were as described in the instructions. The cDNA synthesis was carried out according to the literature [Kato, S. et al., Gene 150: (1994)].

(1) Selection of cDNAs Encoding Proteins HavingHydrophobic Domains

Human liver cDNA library (WO 98/21328) and human stomach cancer cDNA library (WO 98/21328), as well as the cDNA libraries constructed from human kidney mRNA (Clontech), human thymus mRNA (Clontech) and human umbilical cord blood mRNA were used as cDNA libraries.

Full-length cDNA clones were selected from the respective libraries and the whole base sequences thereof determined to construct a homo-protein cDNA of the full-length CDNA clones. The hydrophobicity/hydrophilicity profiles were determined for the proteins encoded by the full-length cDNA registered in the homo-protein cDNA bank by the Kyte-Doolittle method [Kyte, J. & Doolittle, R. F., J. Mol. Biol. 157: 105-132 (1982)] to examine the presence or absence of a hydrophobic domain. A clone that has a hydrophobic region

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being assumed as a secretory signal or a transmembrane domain in the amino acid sequence of the encoded protein was selected as a clone candidate.

(2) Protein Synthesis by In Vitro Translation

The plasmid vector bearing the cDNA of the present invention was used for in vitro transcription/translation with a TT rabbit reticulocyte lysate kit (Promega). In this case, [35S]methionine was added to label the expression product with a radioisotope. Each of the reactions was carried out according to the protocols attached to the kit. Two micrograms of the plasmid was subjected to the reaction at 30°C for 90 minutes in the reaction solution of a total volume of 25  $\mu$ l containing 12.5  $\mu$ l  $\mu$  of  $T_NT$  rabbit reticulocyte lysate,  $0.5~\mu l$  of a buffer solution (attached to the kit), 2 µl of an amino acid mixture (without methionine), 2  $\mu$ l of [35S]methionine (Amersham) (0.37 MBq/ $\mu$ l), 0.5 µl of T7 RNA polymerase, and 20 U of RNasin. The experiment in the presence of a membrane system was carried out by adding 2.5 µl of a canine pancreas microsome fraction (Promega) to the reaction system. To 3 µl of the reaction solution was added 2 µl of the SDS sampling buffer (125 mM Tris-hydrochloride buffer, pH 6.8, 120 mM 2-mercaptoethanol, 2% SDS solution, 0.025% bromophenol blue and 20% glycerol) and the resulting mixture was heated at 95°C for 3 minutes

and then subjected to SDS-polyacrylamide gel electrophoresis.

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The molecular weight of the translation product was determined by carrying out the autoradiography.

### (3) Expression in COS7

Escherichia coli cells harboring the expression vector for the protein of the present invention were cultured at 37°C for 2 hours in 2 ml of the 2 x YT culture medium containing 100  $\mu$ g/ml of ampicillin, the helper phage M13K07 (50  $\mu$  1) was added thereto, and the cells were then cultured at 37°C overnight. Single-stranded phage particles were obtained by polyethylene glycol precipitation from a supernatant separated by centrifugation. The particles were suspended in 100  $\mu$ l of 1 mM Tris-0.1 mM EDTA, pH 8 (TE).

The cultured cells derived from monkey kidney, COS7, were cultured at 37°C in the presence of 5% CO<sub>2</sub> in the Dulbecco's modified Eagle's medium (DMEM) containing 10% fetal calf serum. 1 x 10° COS7 cells were inoculated into a 6-well plate (Nunc, well diameter: 3 cm) and cultured at 37°C for 22 hours in the presence of 5% CO<sub>2</sub>. After the medium was removed, the cell surface was washed with a phosphate buffer solution followed by DMEM containing 50 mM Trishydrochloride (pH 7.5) (TDMEM). A suspension containing 1 µl of the single-stranded phage suspension, 0.6 ml of the DMEM medium and 3 µl of TRANSFECTAM<sup>TM</sup> (IBF) was added to the cells and the cells were cultured at 37°C for 3 hours in the presence of 5% CO<sub>2</sub>. After the sample solution was removed,

the cell surface was washed with TDMEM, 2 ml per well of DMEM containing 10% fetal calf serum was added, and the cells were cultured at 37°C for 2 days in the presence of 5% CO<sub>2</sub>. After the medium was exchanged for a medium containing [35S]cysteine or [35S]methionine, the cells were cultured for one hour. After the medium and the cells were separated each other by centrifugation, proteins in the medium fraction and the cell membrane fraction were subjected to SDS-PAGE.

## (4) Preparation of Antibodies

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A plasmid vector containing the cDNA of the 10 present invention was dissolved in a phosphate buffer solution (PBS: 145 mM NaCl, 2.68 mM KCl, 8.09 mM Na2HPO4, 2 mM KH,PO4, pH 7.2) to a concentration of 2  $\mu$ g/ $\mu$ l. 25  $\mu$ l each (a total of 50 µl) of the thus-prepared plasmid solution in PBS was injected into the right and left musculi quadriceps 15 femoris of three mice (ICR line) using a 26 guage needle. After similar injections were repeated for one month at intervals of one week, blood was collected. The collected blood was stored at 4°C overnight to coagulate the blood, and then centrifuged at  $8,000 \times g$  for five minutes to obtain 20 a supernatant. NaN, was added to the supernatant to a concentration of 0.01% and the mixture was then stored at 4°C. The generation of an antibody was confirmed by immunostaining of COS7 cells into which the corresponding vector had been introduced or by Western blotting using a 25

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cell lysate or a secreted product.

(5) Clone Examples

<HP03171> (SEQ ID NOS: 1, 11 and 21)

Determination of the whole base sequence of the 5 cDNA insert of clone HP03171 obtained from cDNA library of human thymus revealed the structure consisting of a 90-bp 5'-untranslated region, a 804-bp ORF, and a 1148-bp 3'untranslated region. The ORF encodes a protein consisting of amino acid residues and there existed one putative 10 transmembrane domain. Figure 1 depicts the hydrophobicity/hydrophilicity profile, obtained by the Kyte-Doolittle method, of the present protein. In translation resulted in formation of a translation product of 34 kDa that was somewhat larger than the molecular weight 15 of 30,234 predicted from the ORF. In this case, the addition of a microsome led to the formation of a product of 38 kDa. In addition, there exists in the amino acid sequence of this protein one site at which N-glycosylation may occur (Asn-Thr-Thr at position 169).

The search of the protein database using the amino acid sequence of the present protein revealed that the protein was similar to chicken putative transmembrane protein E3-16 (Accession No. AAB70816). Table 3 shows the comparison between amino acid sequences of the human protein of the present invention (HP) and chicken putative

transmembrane protein E3-16 (GG). Therein, the marks of -, \*, and . represent a gap, an amino acid residue identical with that of the protein of the present invention, and an amino acid residue similar to that of the protein of the present invention, respectively. The both proteins shared a homology of 43.0% in the entire region.

Table 3

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HP MVKISFQPAVAGIKGDKADKASASAPAPASATEILLTPAREEQPPQHRSKRGSSVGGVCY 10 . \*. \*. \*.. . .. GG MVKVSFNSALAH--KEAANKEEENSQVL-ILPPDAKEPEDVVVPAGHKRAWCWCM---CF HP LSMGMVVLLMGLVFASVYIYRYFFLAQLARDNFFRCGVLY-EDSL----SSQVRTQM--\*.. .\* \*.....\*. \*. \*\* .. \* . . . \* \*\*. \* \*\*. \* 15 GG ---GLAFMLAGVILGGAYLYKYFAFQQ--GGVYF-CGIKYIEDGLSLPESGAQLKSARYH HP ELEEDVKIYLDENYERINVPVPQFGGGDPADIIHDFQRGLTAYHDISLDKCYVIELNTTI 20 GG TIEQNIQILEEEDVEFISVPVPEFADSDPADIVHDFHRRLTAYLDLSLDKCYVIPLNTSV HP VLPPRNFWELLMNVKRGTYLPQTYIIQEEMVVTEHVSDKEALGSFIYHLCNGKDTYRLRR GG VMPPKNFLELLINIKAGTYLPQSYLIHEQMIVTDRIENVDQLGFFIYRLCRGKETYKLQR WO 01/12660

HP RATRRINKRGAKNCNAIRHFENTFVVETLICGVV

GG KEAMKGIQKREAVNCRKIRHFENRFAMETLICEQ

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Furthermore, the search of the GenBank using the base sequences of the present cDNA has revealed the registration of sequences that shared a homology of 90% or more (for example, Accession No. AL036384) among ESTs. However, since they are partial sequences, it can not be judged whether or not they encode the same protein as the protein of the present invention.

<HP03424> (SEQ ID NOS: 2, 12 and 22)

Determination of the whole base sequence of the cDNA insert of clone HP03424 obtained from cDNA library of human liver revealed the structure consisting of a 4-bp 5'-untranslated region, a 1260-bp ORF, and a 169-bp 3'-untranslated region. The ORF encodes a protein consisting of 419 amino acid residues and there existed a putative secretory signal at the N-terminus and one putative transmembrane domain in the inner portion. Figure 2 depicts the hydrophobicity/hydrophilicity profile, obtained by the Kyte-Doolittle method, of the present protein. In vitro translation resulted in formation of a translation product of 50 kDa that was somewhat larger than the molecular weight

of 46,375 predicted from the ORF. In this case, the addition of a microsome led to the formation of a product of 54 kDa. In addition, there exist in the amino acid sequence of this protein six sites at which N-glycosylation may occur (Asn-Ala-Ser at position 29, Asn-Val-Thr at position 40, Asn-Cys-Thr at position 112, Asn-Lys-Ser at position 135, Asn-Ile-Ser at position 172 and Asn-Phe-Ser at position 189). Application of the (-3,-1) rule, a method for predicting the cleavage site of the secretory signal sequence, allows to expect that the mature protein starts from aspartic acid at position 28.

The search of the protein database using the amino acid sequence of the present protein revealed that the protein was similar to Drosophila melanogaster GOLIATH protein (Accession No. Q06003). Table shows comparison between amino acid sequences of the human protein of the present invention (HP) and Drosophila melanogaster GOLIATH protein (DM). Therein, the marks of -, \*, and . represent a gap, an amino acid residue identical with that of the protein of the present invention, and an amino acid residue similar to that of the protein of the present invention, respectively. The both proteins shared a homology of 40.8% in the intermediate region of 218 amino acid residues.

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|    | Table 4  |
|----|--|
|    | HP MSCAGRAGPARLAALALLTCSLWPARADNASQEYYTALINVTVQEPGRGAPLTFRIDRGR  |
| 5  | HP YGLDSPKAEVRGQVLAPLPLHGVADHLGCDPQTRFFVPPNIKQWIALLQRGNCTFKEKIS  |
|    | HP RAAFHNAVAVVIYNNKSKEEPVTMTHPGTGDIIAVMITELRGKDILSYLEKNISVQMTIA  |
|    | DM MQLEKMQIKGKTRNIAAVITYQNIGQDLSLTLDKGYNVTISII   |
| 10 | HP VGTRMPPKNFSRGSLVFVSISFIVLMIISSAWLIFYFIQKIRYTNARDRNQRRLGDAA  * **. * * * * * * * * * * * * *                                   |
| 15 | HP KKAISKLTTRTVKKGDKETDPDFDHCAVCIESYKQNDVVRILPCKHVFHKSCVDPWLSEH  **** **. * * .* * .* * .* * * * * *                             |
|    | DM KKAIMKIPTKTGKFSD-EKDLDSDCCAICIEAYKPTDTIRILPCKHEFHKNCIDPWLIEH  HP CTCPMCKLNILKALGIVPNLPCTDNVAFDMERLTRTQAVNRRSALGDLAGDNSLGLEPLR |
| 20 | ********** * * *.**.  DM RTCPMCKLDVLKFYGYVVGDQIYQTPSPQHTAPIASIEEVPVIVVAVPHGPQPLQPLQ  |
|    | HP TSGISPLPQDGELTPRTGEINIAVTKEWFIIASFGLLSALTLCYMIIRATASLNANEVEW .**  |

 ${\tt DM} \ \ {\tt ASNMSSFAPSHYFQSSRSPSSSVQQQLAPLTYQPHPQQAASERGRRNSAPATMPHAITAS}$ 

HP F

DM HQVTDV

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Furthermore, the search of the GenBank using the base sequences of the present cDNA has revealed the registration of sequences that shared a homology of 90% or more (for example, Accession No. AA082118) among ESTs. However, since they are partial sequences, it can not be judged whether or not they encode the same protein as the protein of the present invention.

<HP03444> (SEQ ID NOS: 3, 13 and 23)

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Determination of the whole base sequence of the cDNA insert of clone HP03444 obtained from cDNA library of human kidney revealed the structure consisting of a 209-bp 5'-untranslated region, a 1248-bp ORF, and a 460-bp 3'-untranslated region. The ORF encodes a protein consisting of 415 amino acid residues and there existed a putative secretory signal at the N-terminus. Figure 3 depicts the hydrophobicity/hydrophilicity profile, obtained by the Kyte-Doolittle method, of the present protein. In vitro translation resulted in formation of a translation product of 43 kDa that was somewhat smaller than the molecular

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weight of 45,691 predicted from the ORF. In this case, the addition of a microsome led to the formation of a product of 42 kDa. Application of the (-3,-1) rule, a method for predicting the cleavage site of the secretory signal sequence, allows to expect that the mature protein starts from glutamine at position 24.

The search of the protein database using the amino acid sequence of the present protein revealed that the protein was similar to human type I procollagen C-proteinase enhancer protein (Accession No. BAA23281). Table 5 shows the comparison between amino acid sequences of the human protein of the present invention (HP) and human type I procollagen C-proteinase enhancer protein (CP). Therein, the marks of -, \*, and . represent a gap, an amino acid residue identical with that of the protein of the present invention, and an amino acid residue similar to that of the protein of the present invention, respectively. The both proteins shared a homology of 43.6% in the entire region.

20 Table 5

CP MLPAATASLLGPLLTACALLPFA-Q-GQTPNYTRPVFLCGGDVKGESGYVASEGFPNLYP

HP MRGANAWAPLCLLLAAATQLSRQQSPERPVFTCGGILTGESGFIGSEGFPGVYP

\* \*\*. \* \* ..... \*\*\*\* \*\*\*... \*\*\*\*\*... \*\*\*\*\*... \*\*\*\*\*...\*\*

|    | НР | PNSKCTWKITVPEGKVVVLNFRFIDLESDNLCRYDFVDVYNGH-ANGQRIGRFCGTFRPG         |
|----|----|--|
|    |    | **. * * * * * * * * * * * * * * * * * *                              |
|    | CP | ${\tt PNKECIWTITVPEGQTVSLSFRVFDLELHPACRYDALEVFAGSGTSGQRLGRFCGTFRPA}$ |
| 5  | НР | ALVSSGNKMMVQMISDANTAGNGFMAMFSAAEPNERGDQYCGGLLDRPSGSFKTPNWPDR         |
|    |    | ·**. **. · . *. · *. · *. · *. · . · · · ·                           |
|    | CP | PLVAPGNQVTLRMTTDEGTGGRGFLLWYSGRATSGTEHQFCGGRLEKAQGTLTTPNWPES         |
|    |    |  |
|    | HP | DYPAGVTCVWHIVAPKNQLIELKFEKFDVERDNYCRYDYVAVFNGGEVNDARRIGKYCGD         |
| 10 |    | ***. *. * ***. ** . *. *. *. *****. *. *                             |
|    | СР | DYPPGISCSWHIIAPPDQVIALTFEKFDLEPDTYCRYDSVSVFNGAVSDDSRRLGKFCGD         |
|    |    |  |
|    | ΗР | SPPAPIVSERNELLIQFLSDLSLTADGFIGHYIFRPKKLPTTTE                         |
|    |    | *. * ** *** *** ** * * * *   |
|    |    |  |
| 15 | CP | AVPGSISSEGNELLVQFVSDLSVTADGFSASYKTLPRGTAKEGQGPGPKRGTEPKVKLPP         |
|    |    |  |
|    | HP | QPVTTTFPVTTGLKTTVALCQQKCRRTGTLEGNYCSSDFVLAGTVITTITRDG-SLHATV         |
|    |    | * * * * * . * . *  |
|    | CP | KSQPPEKTEESPSAPDAPTCPKQCRRTGTLQSNFCASSLVVTATVKSMVREPGEGLAVTV         |
| 20 |    |  |
|    | ΗР | SIINIYKEGNLAIQQAGKNMSARLTVVCKQCPLLRRGLNYIIMGQVGEDGRGKIM-PNSF         |
|    |    | *. *. **. *. * * * ***** * *. *                                      |
|    | CD | SLIGAYKTGGLDLPSPPTGASLKFYVPCKQCPPMKKGVSYLLMGQV-EENRGPVLPPESF         |
|    | Cr | PTTAVIVIAGENELSI I TAVOPULIAL OLÆGELMUVAASIFFWAÄA-EGMUVALAPELESI.    |

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... ......\*..\*..\*

### CP VVLHRPNQDQILTNLSKRKCPSQPVRAAASQD

The search of the GenBank using the base sequences of the present cDNA has revealed the registration of sequences that shared a homology of 90% or more (for example, Accession No. D78874) among ESTs. However, since they are partial sequences, it can not be judged whether or not they encode the same protein as the protein of the present invention.

<HP03478> (SEQ ID NOS: 4, 14 and 24)

Determination of the whole base sequence of the cDNA insert of clone HP03478 obtained from cDNA library of human umbilical cord blood revealed the structure consisting of a 224-bp 5'-untranslated region, a 1143-bp ORF, and a 891-bp 3'-untranslated region. The ORF encodes a protein consisting of 380 amino acid residues and there existed five putative transmembrane domains. Figure 4 depicts the hydrophobicity/hydrophilicity profile, obtained by the Kyte-Doolittle method, of the present protein. In vitro translation resulted in formation of a translation product of high molecular weight.

The search of the protein database using the amino acid sequence of the present protein revealed that the

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protein was similar to Halocynthia roretzi HrPET-1 protein (Accession No. BAA81907). Table 6 shows the comparison between amino acid sequences of the human protein of the present invention (HP) and Halocynthia roretzi HrPET-1 protein (HR). Therein, the marks of -, \*, and . represent a gap, an amino acid residue identical with that of the protein of the present invention, and an amino acid residue similar to that of the protein of the present invention, respectively. The both proteins shared a homology of 36.8% in the entire region.

Table 6

|    | HP | Q-YWYYMIELSFYWSLLFSIASDVKRKDFKEQIIHHVATIILISFSWFANYIRAGTLIMA |
|----|----|--|
|    |    | . *. **. ***. ** ****** * . *** *. *                         |
|    | HR | KIYYYYLIELAFYSATTLTQFFDVKRKDFWEMFIHHIVTIILLCGSYTLNYTKMGAFILV |
| 5  | НР | LHDSSDYLLESAKMFNYAGWKNTCNNIFIVFAIVFIITRLVILPFWILHCTLVYPLELYP |
|    |    | .***.** *** .** * ** * *****. ** * . *                       |
|    | HR | VHDSADFYIEFAKMGKYANNSLVTNVGFISFTISFFLSRLVILPLWIVPSIWFYGIYTYN |
|    | НР | AFFGYYFFNSMMGVLQLLHIFWAYLILRMAHKFITGKLVEDERSDREETESSEGEEAAAG |
| 10 |    | ********************************                             |
|    | HR | CAMA-WLFCALL-ILQLLHFYWFSHIVKAAYASILVGVIERDTRSESEDSSAEDETAKYS |
|    |    |  |
|    | HP | GGAKSRPLANGHPILNNNHRKND                                      |
|    |    | *.   |
|    |    |  |

The search of the GenBank using the base sequences of the present cDNA has revealed the registration of sequences that shared a homology of 90% or more (for example, Accession No. T27334) among ESTs. However, since they are partial sequences, it can not be judged whether or not they encode the same protein as the protein of the present invention.

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HR VGSGDYTESNGIHKRVVTAR

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Determination of the whole base sequence of the cDNA insert of clone HP03499 obtained from cDNA library of human kidney revealed the structure consisting of a 129-bp 5'-untranslated region, a 1758-bp ORF, and a 86-bp 3'untranslated region. The ORF encodes a protein consisting of 585 amino acid residues and there existed one putative transmembrane domain at the N-terminus. Figure 5 depicts the hydrophobicity/hydrophilicity profile, obtained by the Kyte-Doolittle method, of the present protein. In translation resulted in formation of a translation product of 63 kDa that was almost identical with the molecular weight of 63,987 predicted from the ORF. In this case, the addition of a microsome led to the formation of a product of 82 kDa. In addition, there exist in the amino acid sequence of this protein five sites at which N-glycosylation may occur (Asn-Ile-Thr at position 89, Asn-Glu-Thr at position 106, Asn-Ala-Thr at position 189, Asn-Arg-Thr at position 220 and Asn-Ala-Thr at position 315).

The search of the protein database using the amino acid sequence of the present protein revealed that the 20 protein was similar to Chinese hamster hypothetical protein No. 7 (Accession A30227). Table shows 2BE2121 comparison between amino acid sequences of the human protein Chinese hamster invention (HP) and of the present hypothetical protein 2BE2121 (CH). Therein, the marks of -, 25

\*, and . represent a gap, an amino acid residue identical with that of the protein of the present invention, and an amino acid residue similar to that of the protein of the present invention, respectively. The both proteins shared a homology of 44.8% in the entire region.

Table 7

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HP MVCREQLSKNQVKWVFAGITCVSVVVIAAIVLAITLRRPGCELEACSPDADMLDYLLSLG
..\*\*\*.\*.

CH SWSENILDYFLRNS

- HP QISRRDALEVTWYHAANSKKAMTAALNSNITVLEADVNVEGLGTANETGVPIMAHPPTIY

  \*\*. \*. \*\*\*\*\*\*\* \*.. \* .\*\*\*\*\*

  CH QITTEDGAEIIWYHAANHKSQMQEALRSAAHMIEADVLLPS—DGSEHGQPIMAHPPEMN

HP NMLISTEVNATQFLALVQEKYPKATLSPGWTTFYMSTSPNRTYTQAMVEKMHELVGGVPQ

\* \*. \*. \*. \*\*. \* . . \*. \* \* \*\*\*\*\* . . . \* . . \* . . . . . . . . . \*

CH NG-SSKVVDAKAFLDTVTSFFPDVTFSLGWTTGWHPEKVNEGYSWTMVKEMDYICSGLTQ

HP RVTFPVRSSMVRAAWPHFSWLLSQSERYSLTLWQAASDPMSVEDLLYVRDNTAVHQVYYD

PCT/JP00/05356

.\*\*\*\*\*...\*\*... \*\*\*...\*. ... \*\*\*...\*. ... \*\*\*...\*. ... \*\*...\*... \*\*...\*\*

CH PVTFPVRAALVRQSCSQLLWLLKKSNRYSLTVWTGKDDSYPTEDLLYIRDYFNKTQVFYD

HP IFEPLLSQFKQLALNATRKPMYYTGGSLIPLLQLPGDDGLNVEWLVPDVQGSGKTATMTL

5 \*.\*\* .\*\*\*

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CH ILEPQSHEFKQAIGI

base sequences of the present cDNA has revealed the registration of sequences that shared a homology of 90% or more (for example, Accession No. R92398) among ESTs. However, since they are partial sequences, it can not be judged whether or not they encode the same protein as the protein of the present invention.

<HP03500> (SEQ ID NOS: 6, 16 and 26)

Determination of the whole base sequence of the cDNA insert of clone HP03500 obtained from cDNA library of human kidney revealed the structure consisting of a 134-bp 5'-untranslated region, a 996-bp ORF, and a 476-bp 3'-untranslated region. The ORF encodes a protein consisting of 331 amino acid residues and there existed one putative transmembrane domain at the N-terminus. Figure 6 depicts the hydrophobicity/hydrophilicity profile, obtained by the Kyte-Doolittle method, of the present protein. In vitro

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translation resulted in formation of a translation product of 38 kDa that was almost identical with the molecular weight of 37,694 predicted from the ORF.

The search of the protein database using the amino acid sequence of the present protein revealed that the amino acid sequence of the protein matched with that of human hypothetical protein (Accession No. AAC05803) in which a region of 62 amino acid residues from glycine at position 88 to lysine at position 149 was deleted.

of the present cDNA has revealed the registration of sequences that shared a homology of 90% or more (for example, Accession No. AA340631) among ESTs. However, since they are partial sequences, it can not be judged whether or not they encode the same protein as the protein of the present invention.

<HP10691> (SEQ ID NOS: 7, 17 and 27)

Determination of the whole base sequence of the cDNA insert of clone HP10691 obtained from cDNA library of human umbilical cord blood revealed the structure consisting of a 246-bp 5'-untranslated region, a 1038-bp ORF, and a 1096-bp 3'-untranslated region. The ORF encodes a protein consisting of 345 amino acid residues and there existed at least two putative transmembrane domains. Figure 7 depicts the hydrophobicity/hydrophilicity profile, obtained by the

Kyte-Doolittle method, of the present protein. In vitro translation resulted in formation of a translation product of high molecular weight.

The search of the protein database using the amino acid sequence of the present protein revealed that the protein was similar to human BB1 protein (Accession No. AAB37433). Table 8 shows the comparison between amino acid sequences of the human protein of the present invention (HP) and human BB1 protein (BB). Therein, the marks of -, \*, and . 10 represent a gap, an amino acid residue identical with that of the protein of the present invention, and an amino acid residue similar to that of the protein of the present invention, respectively. The C-terminal region of 215 amino acid residues of the present protein shared a homology of 15 81.9% with the N-terminal region of human BB1 protein.

Table 8

HP MSPEEWTYLVVLLISIPIGFLFKKAGPGLKRWGAAAVGLGLTLFTCGPHTLHSLVTILGT

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HP WALIQAQPCSCHALALAWTFSYLLFFRALSLLGLPTPTPFTNAVQLLLTLKLVSLASEVQ

HP DLHLAQRKEMASGFSKGPTLGLLPDVPSLMETLSYSYCYVGIMTGPFFRYRTYLDWLEQP

\*\*\*\*\*\*

BB

BB LPRGSASLRPLLRRAWPAPLFGLLFLLSSHLFPLEAVREDAFYARPLPARLFYMIPVFFA

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HP NIDCYSTDFCVRVRDGMRYWNMTVQWWLAQYIYKSAPARSYVLRL

\*\*\*\*\*\*\*\*\*\*\*\*\*

BB NIDCYSTDFCVRVRDGMRYWNMTVQWWLAQYIYKSAPARSYVLRTAWTMLLSAYWHGLHP

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The search of the GenBank using the base sequences of the present cDNA has revealed the registration of sequences that shared a homology of 90% or more (for example, Accession No. W48653) among ESTs. However, since they are partial sequences, it can not be judged whether or not they encode the same protein as the protein of the present invention.

<HP10703> (SEQ ID NOS: 8, 18 and 28)

Determination of the whole base sequence of the cDNA insert of clone HP10703 obtained from cDNA library of human kidney revealed the structure consisting of a 359-bp

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5'-untranslated region, a 270-bp ORF, and a 1388-bp 3'-untranslated region. The ORF encodes a protein consisting of 89 amino acid residues and there existed one putative transmembrane domain. Figure 8 depicts the hydrophobicity/hydrophilicity profile, obtained by the Kyte-Doolittle method, of the present protein. In vitro translation resulted in formation of a translation product of 18 kDa that was larger than the molecular weight of 10,469 predicted from the ORF.

The search of the GenBank using the base sequences of the present cDNA has revealed the registration of sequences that shared a homology of 90% or more (for example, Accession No. T08343) among ESTs. However, since they are partial sequences, it can not be judged whether or not they encode the same protein as the protein of the present invention.

<HP10711> (SEQ ID NOS: 9, 19 and 29)

Determination of the whole base sequence of the cDNA insert of clone HP10711 obtained from cDNA library of human kidney revealed the structure consisting of a 29-bp 5'-untranslated region, a 1221-bp ORF, and a 356-bp 3'-untranslated region. The ORF encodes a protein consisting of 406 amino acid residues and there existed a putative secretory signal at the N-terminus and one putative transmembrane domain at the N-terminus. Figure 9 depicts the

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hydrophobicity/hydrophilicity profile, obtained by the Kyte-Doolittle method, of the present protein. In translation resulted in formation of a translation product of 44 kDa that was almost identical with the molecular weight of 43,836 predicted from the ORF. In this case, the addition of a microsome led to the formation of a product of 58 kDa. In addition, there exist in the amino acid sequence of this protein seven sites at which N-glycosylation may occur (Asn-Ser-Thr at position 65, Asn-Trp-Ser at position 95, Asn-Val-Ser at position 134, Asn-Ile-Thr at position 159, Asn-Gly-Ser at position 187, Asn-Arg-Ser at position 230 and Asn-Leu-Thr at position 333). Application of the (-3,-1)rule, a method for predicting the cleavage site of the secretory signal sequence, allows to expect that the mature protein starts from glutamic acid at position 36.

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The search of the protein database using the amino acid sequence of the present protein revealed that the protein was similar to mouse kidney predominant protein (Accession No. BAA92527). Table 9 shows the comparison between amino acid sequences of the human protein of the present invention (HP) and mouse kidney predominant protein (MM). Therein, the marks of -, \*, and . represent a gap, an amino acid residue identical with that of the protein of the present invention, and an amino acid residue similar to that of the protein of the present invention, respectively. The

both proteins shared a homology of 79.9% in the entire region.

Table 9

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The search of the GenBank using the base sequences of the present cDNA has revealed the registration of sequences that shared a homology of 90% or more (for example, Accession No. AA362394) among ESTs. However, since they are partial sequences, it can not be judged whether or not they encode the same protein as the protein of the present invention.

<HP10712> (SEQ ID NOS: 10, 20 and 30)

Determination of the whole base sequence of the cDNA insert of clone HP10712 obtained from cDNA library of human kidney revealed the structure consisting of a 52-bp 5'-untranslated region, a 579-bp ORF, and a 1064-bp 3'-untranslated region. The ORF encodes a protein consisting of 192 amino acid residues and there existed four putative transmembrane domains. Figure 10 depicts the hydrophobicity/hydrophilicity profile, obtained by the Kyte-

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Doolittle method, of the present protein. In vitro translation resulted in formation of a translation product of high molecular weight.

The search of the protein database using the amino acid sequence of the present protein revealed that the protein was similar to mouse calcium channel gamma 5 subunit (Accession No. CAB86387). Table 10 shows the comparison between amino acid sequences of the human protein of the present invention (HP) and mouse calcium channel gamma 5 subunit (MM). Therein, the marks of -, \*, and . represent a gap, an amino acid residue identical with that of the protein of the present invention, and an amino acid residue similar to that of the protein of the present invention, respectively. The both proteins shared a homology of 75.0% in the entire region.

Table 10

HS HSQCKWVMGSILLLVSFVLSSGGLLGFVILLRNQVTLIGFTLMFWCEFTASFLLFLNAIS

MM RSRRKWAIGSYLLLVAFILSSGGLLTFIILLKNQINLLGFTLMFWCEFTASFLFFLNAAS

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HS GLHINSITHPWE

\*\*\*\*\*. \*. \*\*.

MM GLHINSLTQPWDPPAGTLAYRKRGYDGTSLI

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Furthermore, the search of the GenBank using the base sequences of the present cDNA has revealed the registration of sequences that shared a homology of 90% or more (for example, Accession No. AA910339) among ESTs. However, since they are partial sequences, it can not be judged whether or not they encode the same protein as the protein of the present invention.

<HP03010> (SEQ ID NOS: 31, 41 and 51)

Determination of the whole base sequence of the

CDNA insert of clone HP03010 obtained from cDNA library of
human kidney revealed the structure consisting of a 97-bp

5'-untranslated region, a 1134-bp ORF, and a 320-bp 3'untranslated region. The ORF encodes a protein consisting of
377 amino acid residues and there existed at least eight

putative transmembrane domains. Figure 11 depicts the

hydrophobicity/hydrophilicity profile, obtained by the Kyte-Doolittle method, of the present protein. In vitro translation resulted in formation of a translation product of 42 kDa that was almost identical with the molecular weight of 41,462 predicted from the ORF as well as a translation product of high molecular weight.

The search of the protein database using the amino acid sequence of the present protein revealed that the protein was similar to Arabidopsis thaliana hypothetical protein (Accession No. AAC34490). Table 11 shows the comparison between amino acid sequences of the human protein of the present invention (HP) and Arabidopsis thaliana hypothetical protein (AT). Therein, the marks of -, \*, and . represent a gap, an amino acid residue identical with that of the protein of the present invention, and an amino acid residue similar to that of the protein of the present invention, respectively. The both proteins shared a homology of 42.0% in the entire region other than the N-terminal region.

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Table 11

HP MDSALSDPHNGSAEAGGPTNSTTRPPSTPEGIALAYGSLLLMALLPIFFGALRSVRCARG

AT

|    | нР  | KNASDMPETITSKDAARFPITASCILLGLYLFFKIFSQEYINLLLSMYFFVLGILALSHT  |
|----|-----|---|
|    |     | ** * *** * **.*. **   |
|    | ΑT  | VKDTPPTETMSKEHAMRFPLVGSAMLLSLFLLFKFLSKDLVNAVLTAYFFVLGIVALSAT  |
| 5  |     |   |
|    | HP  | ISPFMNKFFPASFPNRQYQLLFTQGSGENKEEIINYEFDTKDLVCLGLSSIVGVWYLLRK  |
|    |     | . * *   |
|    | AT  | LLPAIRRFLPNPWNDNLIVWRFPYFKSLEVEFTKSQVVAGIPGTFFCAWYAWKK        |
|    |     |   |
| 10 | HP  | HWIANNLFGLAFSLNGVELLHLNNVSTGCILLGGLFIYDVFWVFGTNVMVTVAKSFEAPI  |
|    |     | **. ***. * * * * . * . * . * . *                              |
|    | AT  | HWLANNILGLSFCIQGIEMLSLGSFKTGAILLAGLFFYDIFWVFFTPVMVSVAKSFDAPI  |
|    |     |   |
|    | HP  | KLVFPQDLLEKGLEANNFAMLGLGDVVIPGIFIALLLRFDISLKKNTHTYFYTSFAAYIF  |
| 15 |     | **. **  |
|    | AT  | KLLFPTGDALRPYSMLGLGDIVIPGIFVALALRFDVSRRRQPQ-YFTSAFIGYAV       |
|    | UD  | GLGLTIFIMHIFKHAQPALLYLVPACIGFPVLVALAKGEVTEMFSYEESNPKDPAAVTES  |
|    | пг  |   |
| 20 | ΛТ  | *. *** .*. *. ******* ***                                     |
| 20 | ΛI  | OVILIIVVMENT QAAQIALLIIVIAVIGILASHCIMNGDIRPLLAPDESKIEE KIIDES |
|    | НР  | KEGTEASASKGLEKKEK   |
|    | ••• | **.   |
|    | ΔТ  | KTSEEVNKAHDE  |
| 25 | 111 |   |
|    |     |   |

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Furthermore, the search of the GenBank using the base sequences of the present cDNA has revealed the registration of sequences that shared a homology of 90% or more (for example, Accession No. AA380429) among ESTs. However, since they are partial sequences, it can not be judged whether or not they encode the same protein as the protein of the present invention.

<HP03576> (SEQ ID NOS: 32, 42 and 52)

Determination of the whole base sequence of the cDNA insert of clone HP03576 obtained from cDNA library of human kidney revealed the structure consisting of a 88-bp 5'-untranslated region, a 246-bp ORF, and a 1379-bp 3'untranslated region. The ORF encodes a protein consisting of 81 amino acid residues and there existed two putative 12 depicts the domains. Figure transmembrane hydrophobicity/hydrophilicity profile, obtained by the Kyte-Doolittle method, of the present protein. In translation resulted in formation of a translation product of 20 kDa that was larger than the molecular weight of 9,178 predicted from the ORF.

The search of the protein database using the amino acid sequence of the present protein revealed that the protein was similar to human vacuolar proton ATPase 9 kDa (Accession No. NP 003936). Table 12 shows the comparison

between amino acid sequences of the human protein of the present invention (HP) and human vacuolar proton ATPase 9 kDa (VP). Therein, the marks of -, \*, and . represent a gap, an amino acid residue identical with that of the protein of the present invention, and an amino acid residue similar to that of the protein of the present invention, respectively. The both proteins shared a homology of 71.2% in the entire region.

10 Table 12

HP MTAHSFALPVIIFTTFWGLVGIAGPWFVPKGPNRGVIITMLVATAVCCYLFWLIAILAQL

\*. \*... \*, \*... \*\*\*. \*\*. \*\*\*. \*\*\*\*\*\*\*\*\* \* \*\*\*\*\*\*\*

VP MAYHGLTVPLIVMSVFWGFVGFLVPWFIPKGPNRGVIITMLVTCSVCCYLFWLIAILAQL

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HP NPLFGPQLKNETIWYVRFLWE

\*\*\*\*\*\*\*\*

VP NPLFGPQLKNETIWYLKYHWP

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Furthermore, the search of the GenBank using the base sequences of the present cDNA has revealed the registration of sequences that shared a homology of 90% or more (for example, Accession No. W22566) among ESTs. However, since they are partial sequences, it can not be judged

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whether or not they encode the same protein as the protein of the present invention.

<HP03611> (SEQ ID NOS: 33, 43 and 53)

Determination of the whole base sequence of the cDNA insert of clone HP03611 obtained from cDNA library of human kidney revealed the structure consisting of a 189-bp 5'-untranslated region, a 1464-bp ORF, and a 105-bp 3'untranslated region. The ORF encodes a protein consisting of 487 amino acid residues and there existed eleven putative domains. Figure 13 depicts transmembrane hydrophobicity/hydrophilicity profile, obtained by the Kytethe present protein. Doolittle method, In of translation resulted in formation of a translation product of high molecular weight.

The search of the protein database using the amino acid sequence of the present protein revealed that the protein was similar to human cystine/glutamate transporter (Accession No. BAA82628). Table 13 shows the comparison between amino acid sequences of the human protein of the present invention (HP) and human cystine/glutamate transporter (CG). Therein, the marks of -, \*, and . represent a gap, an amino acid residue identical with that of the protein of the present invention, and an amino acid residue similar to that of the protein of the present invention, respectively. The both proteins shared a homology

of 43.8% in the entire region other than the N-terminal region.

Table 13

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- HP MGDTGLRKRREDEKSIQSQEPKTTSLQKELGLISGISIIVGTIIGS CG MVRKPVVSTISKGGYLQGNVNGRLPSLGNKEPPGQEKVQLKRKVTLLRGVSIIIGTIIGA HP GIFVSPKSVLSNTEAVGPCLIIWAACGVLATLGALCFAELGTMITKSGGEYPYLMEAYGP CG GIFISPKGVLQNTGSVGMSLTIWTVCGVLSLFGALSYAELGTTIKKSGGHYTYILEVFGP HP IPAYLFSWASLIVIKPTSFAIICLSFSEYVCAPFYVGCKPPQIVVKCLAAAAILFISTVN CG LPAFVRVWVELLIIRPAATAVISLAFGRYILEPFFIQCEIPELAIKLITAVGITVVMVLN HP SLSVRLGSYVQNIFTAAKLVIVAIIIISGLVLLAQGNTKNFDNSFEGAQLSVGAISLAFY CG SMSVSWSARIQIFLTFCKLTAILIIIVPGVMQLIKGQTQNFKDAFSGRDSSITRLPLAFY

- - HP ISKPITMHLQMLMEVVPPEEDPE
    .\*. \*\*. \*\*...\*\*\*\* \*.
- 15 CG MSEKITRTLQIILEVVPEEDKL

The search of the GenBank using the base sequences of the present cDNA has revealed the registration of sequences that shared a homology of 90% or more (for example, Accession No. R07056) among ESTs. However, since they are partial sequences, it can not be judged whether or not they encode the same protein as the protein of the present invention.

Determination of the whole base sequence of the cDNA insert of clone HP03612 obtained from cDNA library of human kidney revealed the structure consisting of a 153-bp 5'-untranslated region, a 1128-bp ORF, and a 269-bp 3'untranslated region. The ORF encodes a protein consisting of 375 amino acid residues and there existed seven putative transmembrane domains. Figure 14 depicts the hydrophobicity/hydrophilicity profile, obtained by the Kyte-Doolittle method, of the present protein. In translation resulted in formation of a translation product of 39 kDa that was somewhat larger than the molecular weight of 37,930 predicted from the ORF.

The search of the protein database using the amino acid sequence of the present protein revealed that the protein was similar to human monocarboxylate transporter (Accession No. AAC70919). Table 14 shows the comparison between amino acid sequences of the human protein of the present invention (HP) and human monocarboxylate transporter (MC). Therein, the marks of -, \*, and . represent a gap, an amino acid residue identical with that of the protein of the present invention, and an amino acid residue similar to that of the protein of the present invention, respectively. The both proteins shared a homology of 41.7% in the N-terminal region of 192 amino acid residues.

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# Table 14

|    | НР   | MTPQPAGPPDGGWGWVVAAAAFAINGLSYGLLRSLGLAFPDLAEHFDRSAQDTAW   |
|----|------|---|
|    |      | ·*· ******** *·* *·** · · · · · · · · ·   |
| 5  | MC N | MPPMPSAPPVHPPPDGGWGWIVVGATFISIGFSYAFPKAVTVFFKEIQQIFHTTYSEIAW  |
|    |      | ISALALAVQQAASPVGSALSTRWGARPVVMVGGVLASLGFVFSAFASGLLHLYLGLGLLA  |
|    |      | **. *** ***.* *. ***** **. * .**. * * *** ** ** *** ** ***. |
| 10 |      | GFGWALVFAPALGTLSRYFSRRRVLAVGLALTGNGASSLLLAPALQLLLDTFGWRGALLL *.* * *** * * ***. *   |
|    |      | *.* ****** *. * .* *****  |
| 15 |      | LGAITLHLTPCGALLLPLVLPGDPPAPPRSPLAALGLSLFTRRAFSIFALGTALVGGGYF  |
|    |      | ** *. *.**  LGSLLLNACVAGSLMRPLGPNQTTSKSKNKTGKTEDDSSPKKIKTKKSTWEKVNKYLDFS  |
|    | НР   | VPYVHLAPRFRPGPGGIRSSAGGGRGCDGGCGRPAGLRVAGRPRLGAPPAAAGRIRGSDW  |
| 20 | МС   | LFKHRGFLIYLSGNVIMFLGFFAPIIFPAPYAKDQGIDEYSAAFLLSVMAFVDMFARPSV  |
|    | НР   | AGAVGGGAGARGGRRELGGSPAGRGCGLWAERGELRPAGFRCTPRAGGRRRCGAGHRAG   |
| 25 | МС   | GLIANSKYIRPRIQYFFSFAIMFNGVCHLLCPLAQDYTSLVLYAVFFGLGFGSVSSVLFE  |

### HP DDADEPRGAPGPSPVRLPKG

#### MC TLMDLVGAPRFSSAVGLVTIVECGPVLLGPPLAGKLVDLTGEYKYMYMSCGAIVVAASVW

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The search of the GenBank using the base sequences of the present cDNA has revealed the registration of sequences that shared a homology of 90% or more (for example, Accession No. AI742291) among ESTs. However, since they are partial sequences, it can not be judged whether or not they encode the same protein as the protein of the present invention.

<HP10407> (SEQ ID NOS: 35, 45 and 55)

Determination of the whole base sequence of the

cDNA insert of clone HP10407 obtained from cDNA library of human stomach cancer revealed the structure consisting of a 100-bp 5'-untranslated region, a 1053-bp ORF, and a 332-bp 3'-untranslated region. The ORF encodes a protein consisting of 350 amino acid residues and there existed at least four putative transmembrane domains. Figure 15 depicts the

hydrophobicity/hydrophilicity profile, obtained by the Kyte-

Doolittle method, of the present protein.

The search of the protein database using the amino acid sequence of the present protein revealed that the

protein was longer by 35 amino acid residues at the N-terminus than human hypothetical protein (Accession No. CAB43375).

Furthermore, the search of the GenBank using the base sequences of the present cDNA has revealed the registration of a clone beginning from the 117th base of the present cDNA (Accession No. AL050274).

<HP10713> (SEQ ID NOS: 36, 46 and 56)

Determination of the whole base sequence of the cDNA insert of clone HP10713 obtained from cDNA library of 10 human kidney revealed the structure consisting of a 79-bp 5'-untranslated region, a 2004-bp ORF, and a 611-bp 3'untranslated region. The ORF encodes a protein consisting of 667 amino acid residues and there existed nine putative depicts domains. Figure 16 15 transmembrane hydrophobicity/hydrophilicity profile, obtained by the Kytethe present protein. In Doolittle method, of translation resulted in formation of a translation product of high molecular weight.

20 The search of the protein database using the amino acid sequence of the present protein revealed that the protein was similar to mouse retinoic acid-responsive protein (Accession No. AAC16016). Table 15 shows the comparison between amino acid sequences of the human protein of the present invention (HP) and mouse retinoic acid-

responsive protein (MM). Therein, the marks of -, \*, and . represent a gap, an amino acid residue identical with that of the protein of the present invention, and an amino acid residue similar to that of the protein of the present invention, respectively. The both proteins shared a homology of 74.1% in the entire region.

Table 15

|    | HР | SKGLQSSYSEEYLRNLLCRKKLGSSYH-TSKHGFLSWARVCLRHCIYTPQPGFHLPLKLV   |
|----|----|--|
|    |    | *. ***. ****. ***. ***. * . ** **  |
|    | MM | SQGLQTSYSEKYLRTLLCPKKLDSCSHPASKRSLLSRAWAFSHHSIYTPQPGFRLPLKLV   |
|    |    |  |
| 5  | HP | LSATLTGTAIYQVALLLLVGVVPTIQKVRAGVTTDVSYLLAGFGIVLSEDKQEVVELVKH   |
|    |    | ·*************************************   |
|    | MM | ISATLTGTATYQVALLLLVSVVPTVQKVRAGINTDVSYLLAGFGIVLSEDRQEVVELVKH   |
|    |    |  |
|    | HP | ${\tt HLWALEVCYISALVLSCLLTFLVLMRSLVTHRTNLRALHRGAALDLSPLHRSPHPSRQAIDLSPLHRSPHPSPHPSRQAIDLSPLHRSPHPSRQAIDLSPLHRSPHPSRQAIDLSPLHRSPHPSPHPSRQAIDLSPLHRSPHPSPHPSRQAIDLSPLHRSPHPSPHPSPHPSPHPSPHPSPHPSPHPSPHPSPHPSP$ |
| 10 |    | ***. *. ******** ***. *. ***. **. ******   |
|    | MM | HLWTVEACYISALVLSCASTFLLLIRSLRTHRANLQALHRGAALDLDPPLQSIHPSRQAI   |
|    |    |  |
|    | HP | FCWMSFSAYQTAFICLGLLVQQIIFFLGTTALAFLVLMPVLHGRNLLLFRSLESSWPFWL   |
|    |    | · ****· ****** ******* ****** ****** ******  |
| 15 | ММ | VSWMSFCAYQTAFSCLGLLVQQVIFFLGTTSLAFLVFVPLLHGRNLLLLRSLESTWPFWL   |
|    |    |  |
|    | HP | TLALAVILQNMAAHWVFLETHDGHPQLTNRRVLYAATFLLFPLNVLVGAMVATWRVLLSA   |
|    |    | *. ********. **. *. ** **. *. *. *****. *.   |
|    | ММ | TVALAVILQNIAANWIFLRTHHGYPELTNRRMLCVATFLLFPINMLVGAIMAVWRVLISS   |
| 20 |    |  |
|    | НР | LYNAIHLGQMDLSLLPPRAATLDPGYYTYRNFLKIEVSQSHPAMTAFCSLLLQAQSLLPR   |
|    |    | ***. *********** ***. ***. ***. **. **.  |
|    | ММ | LYNTVHLGQMDLSLLPQRAASLDPGYHTYQNFLRIEASQSHPGVIAFCALLLHAPSPQPR   |
|    |    |  |

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HP ALLGANGAQP

5 **\*\*** . **\***. .

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MM ALTSAKANGTQP

The search of the GenBank using the base sequences

of the present cDNA has revealed the registration of
sequences that shared a homology of 90% or more (for example,
Accession No. AI760170) among ESTs. However, since they are
partial sequences, it can not be judged whether or not they
encode the same protein as the protein of the present

invention.

<HP10714> (SEQ ID NOS: 37, 47 and 57)

Determination of the whole base sequence of the cDNA insert of clone HP10714 obtained from cDNA library of human umbilical cord blood revealed the structure consisting of a 82-bp 5'-untranslated region, a 1395-bp ORF, and a 1820-bp 3'-untranslated region. The ORF encodes a protein consisting of 464 amino acid residues and there existed a putative secretory signal at the N-terminus. Figure 17 depicts the hydrophobicity/hydrophilicity profile, obtained by the Kyte-Doolittle method, of the present protein. In

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vitro translation resulted in formation of a translation product of 49 kDa that was somewhat smaller than the molecular weight of 52,340 predicted from the ORF. In this case, the addition of a microsome led to the formation of a product of 52 kDa. In addition, there exist in the amino acid sequence of this protein two sites at which N-glycosylation may occur (Asn-Ala-Thr at position 164 and Asn-Asp-Ser at position 320). Application of the (-3,-1) rule, a method for predicting the cleavage site of the secretory signal sequence, allows to expect that the mature protein starts from threonine at position 22.

The search of the GenBank using the base sequences of the present cDNA has revealed the registration of sequences that shared a homology of 90% or more (for example, Accession No. AA861134) among ESTs. However, since they are partial sequences, it can not be judged whether or not they encode the same protein as the protein of the present invention.

<HP10716> (SEQ ID NOS: 38, 48 and 58)

Determination of the whole base sequence of the cDNA insert of clone HP10716 obtained from cDNA library of human umbilical cord blood revealed the structure consisting of a 60-bp 5'-untranslated region, a 1413-bp ORF, and a 653-bp 3'-untranslated region. The ORF encodes a protein consisting of 470 amino acid residues and there existed one

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putative transmembrane domain at the N-terminus. Figure 18 depicts the hydrophobicity/hydrophilicity profile, obtained by the Kyte-Doolittle method, of the present protein. In vitro translation resulted in formation of a translation product of 61 kDa that was larger than the molecular weight of 52,086 predicted from the ORF.

The search of the protein database using the amino acid sequence of the present protein revealed that the protein was similar to human hypothetical protein CGI-90 (Accession No. AAD34085). Table 16 shows the comparison between amino acid sequences of the human protein of the present invention (HP) and human hypothetical protein CGI-90 (CG). Therein, the marks of -, \*, and . represent a gap, an amino acid residue identical with that of the protein of the present invention, and an amino acid residue similar to that of the protein of the present invention, respectively. The both proteins shared a homology of 32.4% in the entire region.

20 Table 16

HP MSRLGALGGARAGLGLLLGTAAGLGFLCLLYSQRWKRTQRHGRSQSLPNSLDYTQTSDPG

HP RHVMLLRAVPGGAGDASVLPSLPREGQEKVLDRLDFVLTSLVALRREVEELRSSLRGLAG

|    | HP EIVGEVRCHMEENQRVARRRRFPFVRERSDSTGSSSVYFTASSGATFTDAESEGGYTTAN  |
|----|--|
|    | CG MALAARLWRLLPFRRGAAPGSRLPA   |
| 5  | HP AESDNERDSDKESEDGEDEVSCETVKMGRKDSLDLEEEAASGASSALEAGGSSGLEDVLP  |
|    | CG GPSGSRGIAAPARFRGFEVMGNPGTFNRGLLLSALSYLGFETYQVISQAAVVHATAKVEE  |
| 10 | HP LLQQADELHRGDEQGKREGFQLLLNNKLVYGSRQDFLWRLARAYSDMCELT-EEVSEKKS  .*.*** ** .* .********* .*****  |
|    | CG ILEQADYLYESGETEKLYQLLTQYKESEDAELLWRLARASRDVAQLSRTSEEEKKL  |
|    | HP YALDGKEEAEAALEKGDESADCHLWYAVLCGQLAEHESIQRRIQSGFSFKEHVDKAIALQ  * * *****. * ****. * * ***. ***.  |
| 15 | CG LVYEALEYAKRALEKNESSFASHKWYAICLSDVGDYEGIKAKIANAYIIKEHFEKAIELN  |
|    | HP PENPMAHFLLGRWCYQVSHLSWLEKKTATALLESPLSATVEDALQSFLKAEELQPGFSKA  |
|    | * *. *. * *** * * * *. * * . * * . * * . * * . * |
| 20 |  |
|    | HP GRVYISKCYRELGKNSEARWWMKLALELPDVTKEDLAIQKDLEELEVILRD   |
|    | * * . * . * . * . * . * . * . * .  |
|    | CG NLLLLGKTYLKLHNKKLAAFWLMKAKDYPAHTEEDKQIQTEAAQLLTSFSEKN   |

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The search of the GenBank using the base sequences of the present cDNA has revealed the registration of sequences that shared a homology of 90% or more (for example, Accession No. AA852295) among ESTs. However, since they are partial sequences, it can not be judged whether or not they encode the same protein as the protein of the present invention.

<HP10717> (SEQ ID NOS: 39, 49 and 59)

Determination of the whole base sequence of the cDNA insert of clone HP10717 obtained from cDNA library of human kidney revealed the structure consisting of a 73-bp 5'-untranslated region, a 732-bp ORF, and a 976-bp 3'untranslated region. The ORF encodes a protein consisting of 243 amino acid residues and there existed two putative domains. 19 transmembrane Figure depicts the hydrophobicity/hydrophilicity profile, obtained by the Kyte-Doolittle method, of the present protein. In translation resulted in formation of a translation product of 36 kDa that was larger than the molecular weight of 26,270 predicted from the ORF.

The search of the GenBank using the base sequences of the present cDNA has revealed the registration of sequences that shared a homology of 90% or more (for example, Accession No. AI478174) among ESTs. However, since they are partial sequences, it can not be judged whether or not they

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encode the same protein as the protein of the present invention.

<HP10718> (SEQ ID NOS: 40, 50 and 60)

Determination of the whole base sequence of the cDNA insert of clone HP10718 obtained from cDNA library of human umbilical cord blood revealed the structure consisting of a 86-bp 5'-untranslated region, a 813-bp ORF, and a 889bp 3'-untranslated region. The ORF encodes consisting of 270 amino acid residues and there existed three putative transmembrane domains. Figure 20 depicts the hydrophobicity/hydrophilicity profile, obtained by the Kytethe present protein. Doolittle method, In of translation resulted in formation of a translation product of 28 kDa that was smaller than the molecular weight of 31,116 predicted from the ORF.

The search of the protein database using the amino acid sequence of the present protein revealed that the protein was similar to Caenorhabditis elegans hypothetical protein Y53C10A (Accession No. CAA22139). Table 17 shows the comparison between amino acid sequences of the human protein of the present invention (HP) and Caenorhabditis elegans hypothetical protein Y53C10A (CE). Therein, the marks of -, \*, and . represent a gap, an amino acid residue identical with that of the protein of the present invention, and an amino acid residue similar to that of the protein of the

present invention, respectively. The both proteins shared a homology of 54.8% in the entire region other than the N-terminal region.

5 Table 17

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HP MAGAEDWPGQ

- CE MTSSSAASSSTTTSSTMMPDENECLKKEEERFKSPDPAPTLDEEVDIDTLPSMLEDDPNG
- HP QLELDEDEASCCRWGAQHAGARELAALYSPGKRLQEWCSVILCFSLIAHNLVHLLLLARW
  - CE NVVECDLGFKGPRWGPQHAGAKKLASMYSKEKRLQEKVSLFAAIFLFSIVFIN-LLLS-W
- - CE ESSIWVSVLVSAVLGIMTADFASGLVHWAADTFGSVE-TWFGRSFIRPFREHHVDPTAIT
  - HP RHDFIETNGDNCLVTLLPLLNMAYKFRTHSPEALEQ-LYPWECFVFCLIIFGTFTNQIH
- 20 \*\*\*..\*.\*\*\*\*... \*\*\* . \*. . \* ... \* \* ... \* \* ... \*\*\*
  - CE RHDIVEVNGDNCMLCVGPLLWILYQQMTYQRDAITQWATFHW--YILLLGIYVALTNQIH
- 25 CE KWSHTYFGLPTWVVFLQKAHIILPRSHHKIHHISPHACYYCITTGWLNWPLEYIGFWRKM

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HP EDLIQGLTGEKPRADDMKWAQKIK

\* .. .. \*\* . \*\*. \*\*. \*\*\* \*..

CE EWYVTTVTGMQPREDDLKWATKLQ

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Furthermore, the search of the GenBank using the base sequences of the present cDNA has revealed the registration of sequences that shared a homology of 90% or more (for example, Accession No. AA176107) among ESTs. However, since they are partial sequences, it can not be judged whether or not they encode the same protein as the protein of the present invention. In addition, the region from position 466 to position 778 of the cDNA of the present invention matched with the region from position 2 to position 314 of human ubiquitin-conjugating enzyme E2 variant 1 (Accession NO. NM\_003349) although no match was observed in another region.

<HP03745> (SEQ ID NOS: 61, 71 and 81)

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Determination of the whole base sequence of the cDNA insert of clone HP03745 obtained from cDNA library of human kidney revealed the structure consisting of a 99-bp 5'-untranslated region, a 1170-bp ORF, and a 107-bp 3'-untranslated region. The ORF encodes a protein consisting of 389 amino acid residues and there existed at least nine

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putative transmembrane domains. Figure 21 depicts the hydrophobicity/hydrophilicity profile, obtained by the Kyte-Doolittle method, of the present protein. In vitro translation resulted in formation of a translation product of high molecular weight.

The search of the protein database using the amino acid sequence of the present protein revealed that the protein was similar to human solute carrier family 7 (Accession No. NP\_003974). Table 18 shows the comparison between amino acid sequences of the human protein of the present invention (HP) and human solute carrier family 7 (SC). Therein, the marks of -, \*, and . represent a gap, an amino acid residue identical with that of the protein of the present invention, and an amino acid residue similar to that of the protein of the present invention, respectively. The both proteins shared a homology of 36.0% in the N-terminal region of 397 amino acid residues.

Table 18

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HP

MDRGEKIQLKRVFGYWWGTSFLLINIIG

.\*. \*\*\*. .. \*. \*. \*. \*. \*\*

SC MEAREPGRPTPTYHLVPNTSQSQVEEDVSSPPQRSSETMQLKKEISLLNGVSLVVGNMIG

|    | · *********** · · · · · · · · · · · · ·                         |
|----|---|
|    | SC SGIFVSPKGVLVHT-ASYGMSLIVWAIGGLFSVVGALCYAELGTTITKSGASYAYILEAF |
|    | HP GSTVAFLNLWTSLFLGSGVVAG-QALLLAEYSIQPFFPSCSVPKLPKKCLALAMLWIVGI |
| 5  | * ** **   |
|    | SC GGFIAFIRLWVSLLVVEPTGQAIIAITFANYIIQPSFPSCDPPYLACRLLAAACICLLTF |
|    | HP LTSRGVKEVTWLQIASSVLKVSILSFISLTGVVFLIRGKKENVERFQNAFDAELPDISHL |
|    | ** ** . ** * * . *.* . *.**. ** **                              |
| 10 | SC VNCAYVKWGTRVQDTFTYAKVVALIAIIVMGLVKLCQGHSEHFQDAFEGSSWDMGNL    |
|    | HP IQAIFQGYFAYSGELKKPRTTIPKCIFTALPLVTVVYLLVNISYLTVLTPR          |
|    | **.***  |
|    | SC SLALYSALFSYSGWDTLNFVTEEIKNPERNLPLAIGISMPIVTLIYILTNVAYYTVLNIS |
| 15 |   |
|    | HP EILSSDAVAITWADRAFPSLAWIMPFAISTSLFSNLLISIFKSSRPIYLASQEGQLPLLF |
|    | ··************************************                          |
|    | SC DVLSSDAVAVTFADQTFGMFSWTIPIAVALSCFGGLNASIFASSRLFFVGSREGHLPDLL |
| 20 | HP NTLNSHS-SPFTAVLLLVTLGSLAIILTSLIDLINYIFFTGSLWSILLMIGILRRRYQEF |
|    |   |
|    | SC SMIHIERFTPIPALLFNCTMALIYLIVEDVFQLINYFSFSYWFFVGLSVVGQLYLRWKEF |
|    | HP NLSIPYKVKLDF   |
|    |   |
| 25 | * * *   |

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## SC KRPRPLKLSVFFPIVFCICSVFLVIVPLFTDTINSLIGIGIALSGVPFYFMGVYLPESRR

#### <HP03747> (SEQ ID NOS: 62, 72 and 82)

Determination of the whole base sequence of the cDNA insert of clone HP03747 obtained from cDNA library of human umbilical cord blood revealed the structure consisting of a 21-bp 5'-untranslated region, a 1047-bp ORF, and a 1324-bp 3'-untranslated region. The ORF encodes a protein consisting of 348 amino acid residues and there existed a putative secretory signal at the N-terminus and one putative transmembrane domain at the C-terminus. Figure 22 depicts the hydrophobicity/hydrophilicity profile, obtained by the Kyte-Doolittle method, of the present protein. In vitro translation resulted in formation of a translation product of 40 kDa that was almost identical with the molecular weight of 39,685 predicted from the ORF. Application of the (-3,-1) rule, a method for predicting the cleavage site of the secretory signal sequence, allows to expect that the mature protein starts from proline at position 39.

The search of the protein database using the amino acid sequence of the present protein revealed that the protein was similar to human endoplasmic reticulum glycoprotein (Accession No. NP\_006807). Table 19 shows the comparison between amino acid sequences of the human protein

of the present invention (HP) and human endoplasmic reticulum glycoprotein (ER). Therein, the marks of -, \*, and . represent a gap, an amino acid residue identical with that of the protein of the present invention, and an amino acid residue similar to that of the protein of the present invention, respectively. The both proteins shared a homology of 54.1% in the entire region.

Table 19

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- ER MAAEGWIWRWGWGRRCLGRPGLLGPGPGPTTPLFLLLL-LGSVTADITDGNS-EHLK
- HP VHFKIHGQGKKNLHGDGLAIWYTKDRMQPGPVFGNMDKFVGLGVFVDTYPNEEKQQERVF

  \*\*\*\*. \*\* \*\*\*\*\*\*\*\*. \*. \*\*\*\*\*\*. \*. \* \*\*. \* \*\*. \* \*\*\*\*

  ER VHFKVHGTGKKNLHGDGIALWYTRDRLVPGPVFGSKDNFHGLAIFLDTYPNDET-TERVF

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ER RFY

15 Furthermore, the search of the GenBank using the base sequences of the present cDNA has revealed the registration of sequences that shared a homology of 90% or more (for example, Accession No. AA262924) among ESTs. However, since they are partial sequences, it can not be judged whether or not they encode the same protein as the protein of the present invention.

<HP10719> (SEQ ID NOS: 63, 73 and 83)

Determination of the whole base sequence of the cDNA insert of clone HP10719 obtained from cDNA library of human kidney revealed the structure consisting of a 54-bp

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5'-untranslated region, a 786-bp ORF, and a 576-bp 3'-untranslated region. The ORF encodes a protein consisting of 261 amino acid residues and there existed a putative secretory signal at the N-terminus and one putative transmembrane domain in the inner portion. Figure 23 depicts the hydrophobicity/hydrophilicity profile, obtained by the Kyte-Doolittle method, of the present protein. In vitro translation resulted in formation of a translation product of 33 kDa that was larger than the molecular weight of 27,435 predicted from the ORF. Application of the (-3,-1) rule, a method for predicting the cleavage site of the secretory signal sequence, allows to expect that the mature protein starts from asparagine at position 19.

acid sequence of the present protein revealed that the protein was similar to mouse endomucin (Accession No. AAD05208). Table 20 shows the comparison between amino acid sequences of the human protein of the present invention (HP) and mouse endomucin (MM). Therein, the marks of -, \*, and .

20 represent a gap, an amino acid residue identical with that of the protein of the present invention, and an amino acid residue similar to that of the protein of the present invention, respectively. The both proteins shared a homology of 47.9% in the entire region.

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Table 20

|    | НР | MELLQVTIL-FLLP-SIC-SSNSTGVL-EAANNSLVVTTTKPSITTPNTESLQKNVVTPT |
|----|----|--|
|    |    | * ***. *. * ***. *. *  |
| 5  | MM | MRLLQATVLFFLLSNSLCHSEDGKDVQNDSIPTPAETSTTKASVTIPGIVSV-TNPNKPA |
|    |    |  |
|    | НР | TGTTPKGTITNELLKMSLMSTATFLTSKDEGLKATTTDVRKNDSIISNVTVTSVTLPNAV |
|    |    | .**.*.** ************  |
|    | MM | DGTPPEGTTKSDVSQTSLVTTINSLTTPKHEVGTTTEGPLRNESSTMKITVPNTPTSNAN |
| 10 |    |  |
|    | НР | STLQSSKPKTETQSSIKTTEIPGSVLQPDASPSKTGTLTSIPVTIPENTSQSQVIGTEGG |
|    |    | ****. *** ***.   |
|    | ММ | STLPGSQNKITTQLLDALPKITATPSASLTTAHTMSLLQDTEDR                 |
|    |    |  |
| 15 | HP | KNASTSATSRSYSSIILPVVIALIVITLSVFVLVGLYRMCWKADPGTPENGNDQPQSDKE |
|    |    | * *. * * ************************                            |
|    | MM | KIATTPSTTPSYSSIILPVVIALVVITLLVFTLVGLYRICWKRDPGTPENGNDQPQSDKE |
|    |    |  |
|    | HP | SVKLLTVKTISHESGEHSAQGKTKN                                    |
| 20 |    | ***********  |
|    | ММ | SVKLLTVKTISHESGEHSAQGKTKN                                    |
|    |    |  |

The search of the GenBank using the base sequences of the present cDNA has revealed the registration of

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sequences that shared a homology of 90% or more (for example, Accession No. AA486620) among ESTs. However, since they are partial sequences, it can not be judged whether or not they encode the same protein as the protein of the present invention.

<HP10720> (SEQ ID NOS: 64, 74 and 84)

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Determination of the whole base sequence of the cDNA insert of clone HP10720 obtained from cDNA library of human kidney revealed the structure consisting of a 25-bp 5'-untranslated region, a 669-bp ORF, and a 653-bp @3'untranslated region. The ORF encodes a protein consisting of 222 amino acid residues and there existed a putative secretory signal at the N-terminus and one putative transmembrane domain in the inner portion. Figure 24 depicts the hydrophobicity/hydrophilicity profile, obtained by the Kyte-Doolittle method, of the present protein. In vitro translation resulted in formation of a translation product of 28 kDa that was somewhat larger than the molecular weight of 25,219 predicted from the ORF. In this case, the addition of a microsome led to the formation of a product of 35 kDa. In addition, there exist in the amino acid sequence of this protein two sites at which N-glycosylation may occur (Asn-Val-Thr at position 76 and Asn-His-Thr at position 93). Application of the (-3,-1) rule, a method for predicting the cleavage site of the secretory signal sequence, allows to

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expect that the mature protein starts from glutamic acid at position 15.

The search of the GenBank using the base sequences of the present cDNA has revealed the registration of sequences that shared a homology of 90% or more (for example, Accession No. AI792241) among ESTs. However, since they are partial sequences, it can not be judged whether or not they encode the same protein as the protein of the present invention.

10 <HP10721> (SEQ ID NOS: 65, 75 and 85)

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Determination of the whole base sequence of the cDNA insert of clone HP10721 obtained from cDNA library of human kidney revealed the structure consisting of a 74-bp 5'-untranslated region, a 552-bp ORF, and a 1658-bp 3'-15 untranslated region. The ORF encodes a protein consisting of amino acid residues and there existed a putative secretory signal at the N-terminus and one putative transmembrane domain in the inner portion. Figure 25 depicts the hydrophobicity/hydrophilicity profile, obtained by the 20 Kyte-Doolittle method, of the present protein. In vitro translation resulted in formation of a translation product of 23 kDa that was somewhat larger than the molecular weight of 19,989 predicted from the ORF. In this case, the addition of a microsome led to the formation of a product of 22 kDa. 25 Application of the (-3,-1) rule, a method for predicting the

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cleavage site of the secretory signal sequence, allows to expect that the mature protein starts from glutamic acid at position 25.

The search of the GenBank using the base sequences of the present cDNA has revealed the registration of sequences that shared a homology of 90% or more (for example, Accession No. R27187) among ESTs. However, since they are partial sequences, it can not be judged whether or not they encode the same protein as the protein of the present invention.

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## <HP10725> (SEQ ID NOS: 66, 76 and 86)

Determination of the whole base sequence of the cDNA insert of clone HP10725 obtained from cDNA library of human kidney revealed the structure consisting of a 235-bp 5'-untranslated region, a 789-bp ORF, and a 713-bp 3'untranslated region. The ORF encodes a protein consisting of 262 amino acid residues and there existed one putative depicts the 26 domain. Figure transmembrane hydrophobicity/hydrophilicity profile, obtained by the Kytethe present protein. In Doolittle method, of translation resulted in formation of a translation product of high molecular weight.

The search of the GenBank using the base sequences of the present cDNA has revealed the registration of sequences that shared a homology of 90% or more (for example,

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Accession No. AI127782) among ESTs. However, since they are partial sequences, it can not be judged whether or not they encode the same protein as the protein of the present invention.

<HP10727> (SEQ ID NOS: 67, 77 and 87)

Determination of the whole base sequence of the cDNA insert of clone HP10727 obtained from cDNA library of human umbilical cord blood revealed the structure consisting of a 102-bp 5'-untranslated region, a 507-bp ORF, and a 947-3'-untranslated region. The ORF encodes a protein consisting of 168 amino acid residues and there existed a putative secretory signal at the N-terminus and one putative transmembrane domain in the inner portion. Figure 27 depicts the hydrophobicity/hydrophilicity profile, obtained by the Kyte-Doolittle method, of the present protein. In vitro translation resulted in formation of a translation product of 24 kDa that was larger than the molecular weight of 17,822 predicted from the ORF. In this case, the addition of a microsome led to the formation of a product of 23 kDa. Application of the (-3,-1) rule, a method for predicting the cleavage site of the secretory signal sequence, allows to expect that the mature protein starts from lysine at position 29.

The search of the GenBank using the base sequences of the present cDNA has revealed the registration of

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sequences that shared a homology of 90% or more (for example, Accession No. R80316) among ESTs. However, since they are partial sequences, it can not be judged whether or not they encode the same protein as the protein of the present invention.

<HP10728> (SEQ ID NOS: 68, 78 and 88)

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Determination of the whole base sequence of the cDNA insert of clone HP10728 obtained from cDNA library of human umbilical cord blood revealed the structure consisting of a 221-bp 5'-untranslated region, a 732-bp ORF, and a 902-bp 3'-untranslated region. The ORF encodes a protein consisting of 243 amino acid residues and there existed one putative transmembrane domain at the N-terminus. Figure 28 depicts the hydrophobicity/hydrophilicity profile, obtained by the Kyte-Doolittle method, of the present protein. In vitro translation resulted in formation of a translation product of 30 kDa that was larger than the molecular weight of 26,534 predicted from the ORF.

of the present cDNA has revealed the registration of sequences that shared a homology of 90% or more (for example, Accession No. H23535) among ESTs. However, since they are partial sequences, it can not be judged whether or not they encode the same protein as the protein of the present invention.

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## <HP10730> (SEQ ID NOS: 69, 79 and 89)

Determination of the whole base sequence of the cDNA insert of clone HP10730 obtained from cDNA library of human umbilical cord blood revealed the structure consisting of a 27-bp 5'-untranslated region, a 1287-bp ORF, and a 1216-bp 3'-untranslated region. The ORF encodes a protein consisting of 428 amino acid residues and there existed one putative transmembrane domain. Figure 29 depicts hydrophobicity/hydrophilicity profile, obtained by the Kyte-Doolittle method, of the present protein. In translation resulted in formation of a translation product of 50 kDa that was somewhat larger than the molecular weight of 48,992 predicted from the ORF.

The search of the GenBank using the base sequences of the present cDNA has revealed the registration of sequences that shared a homology of 90% or more (for example, Accession No. C19105) among ESTs. However, since they are partial sequences, it can not be judged whether or not they encode the same protein as the protein of the present invention.

## <HP10742> (SEQ ID NOS: 70, 80 and 90)

Determination of the whole base sequence of the cDNA insert of clone HP10742 obtained from cDNA library of human umbilical cord blood revealed the structure consisting of a 231-bp 5'-untranslated region, a 852-bp ORF, and a 828-

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bp 3'-untranslated region. The ORF encodes a protein consisting of 283 amino acid residues and there existed two putative transmembrane domains. Figure 30 depicts the hydrophobicity/hydrophilicity profile, obtained by the Kyte-Doolittle method, of the present protein. In vitro translation resulted in formation of a translation product of 30 kDa that was smaller than the molecular weight of 31,629 predicted from the ORF.

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Furthermore, the search of the GenBank using the base sequences of the present cDNA has revealed the registration of sequences that shared a homology of 90% or more (for example, Accession No. T35949) among ESTs. However, since they are partial sequences, it can not be judged whether or not they encode the same protein as the protein of the present invention.

<HP03800> (SEQ ID NOS: 91, 101 and 111)

Determination of the whole base sequence of the cDNA insert of clone HP03800 obtained from cDNA library of human umbilical cord blood revealed the structure consisting of a 67-bp 5'-untranslated region, a 1431-bp ORF, and a 135-bp 3'-untranslated region. The ORF encodes a protein consisting of 476 amino acid residues and there existed a putative secretory signal at the N-terminus. Figure 31 depicts the hydrophobicity/hydrophilicity profile, obtained by the Kyte-Doolittle method, of the present protein. In

vitro translation resulted in formation of a translation product of 55 kDa that was almost identical with the molecular weight of 54,110 predicted from the ORF. In this case, the addition of a microsome led to the formation of a product of 58 kDa. In addition, there exist in the amino acid sequence of this protein four sites at which N-glycosylation may occur (Asn-Lys-Thr at position 81, Asn-Met-Thr at position 132, Asn-Val-Thr at position 307 and Asn-Gln-Thr at position 346). Application of the (-3,-1) rule, a method for predicting the cleavage site of the secretory signal sequence, allows to expect that the mature protein starts from leucine at position 23.

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The search of the protein database using the amino acid sequence of the present protein revealed that the similar protein was to mosquito vitellogenic carboxypeptidase (Accession No. P42660). Table 21 shows the comparison between amino acid sequences of the human protein of the present invention (HP) and mosquito vitellogenic carboxypeptidase (VC). Therein, the marks of -, \*, and . represent a gap, an amino acid residue identical with that of the protein of the present invention, and an amino acid residue similar to that of the protein of the present invention, respectively. The both proteins shared a homology of 44.5% in the entire region. In addition, the C-terminal portion beginning from alanine at position 182 matched with human probable carboxypeptidase (Accession No. AAC23787) except one amino acid residue.

Table 21

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- HP DLYSALIQFFQIFPEYKNNDFYVTGESYAGKYVPAIAHLIHSLNPVREVKINLNGIAIGD
  .\*..\*\*\*.\*\*...\*\*...\*\* \*... \*\*\*\*.\*\*\*
  VC NLMKFIQQFFVLFPNLLKHPFYISGESYGGKFVPAFGYAIH--NSQSQPKINLQGLAIGD

- HP AEKKVWKIFKSDSEVAGYIRQAGDFHQVIIRGGGHILPYDQPLRAFDMINRFIYGKGWDP

  \*... \*.. \*. \*\*\* ... \*\*\* ... \* \*\*\* ... \*\*\*\*

  VC ANRE---IYRVDGEIAGYKKRAGRLQEVLIRNAGHMVPRDQPKWAFDMITSFTHKNYL

HP YVG

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The search of the GenBank using the base sequences of the present cDNA has revealed the registration of sequences that shared a homology of 90% or more (for example, Accession No. AA095665) among ESTs. However, since they are partial sequences, it can not be judged whether or not they encode the same protein as the protein of the present invention.

<HP03831> (SEQ ID NOS: 92, 102 and 112)

Determination of the whole base sequence of the cDNA insert of clone HP03831 obtained from cDNA library of

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human kidney revealed the structure consisting of a 191-bp 5'-untranslated region, a 681-bp ORF, and a 223-bp 3'-untranslated region. The ORF encodes a protein consisting of 226 amino acid residues and there existed four putative transmembrane domains. Figure 32 depicts the hydrophobicity/hydrophilicity profile, obtained by the Kyte-Doolittle method, of the present protein. In vitro translation resulted in formation of a translation product of high molecular weight.

The search of the protein database using the amino acid sequence of the present protein revealed that the protein was similar to human claudin-10 (Accession No. NP\_008915). Table 22 shows the comparison between amino acid sequences of the human protein of the present invention (HP) and human claudin-10 (CD). Therein, the marks of -, \*, and . represent a gap, an amino acid residue identical with that of the protein of the present invention, and an amino acid residue similar to that of the protein of the present invention, respectively. The both proteins shared a homology of 76.2% in the entire region. The C-terminal region downstream from glycine at position 72 completely matched with that sequence.

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|    | HP | MSRAQIWALVSGVGGFGALVAATTSNEWKVTTRASSVITATWVYQGLWMNCAGNALGS   |
|----|----|--|
|    |    | * ** ***.* ***. * *  |
|    | CD | MASTASEIIAFMVSISGWVLVSSTLPTDYWKVSTIDGTVITTATYWANLWKACVTDSTGV |
|    |    |  |
| 5  | HP | FHCRPHFTIFKVAGYIQACRGLMIAAVSLGFFGSIFALFGMKCTKVGGSDKAKAKIACLA |
|    |    | . * ***************************                              |
|    | CD | SNCKDFPSMLALDGYIQACRGLMIAAVSLGFFGSIFALFGMKCTKVGGSDKAKAKIACLA |
|    |    |  |
|    | HP | GIVFILSGLCSMTGCSLYANKITTEFFDPLFVEQKYELGAALFIGWAGASLCIIGGVIFC |
| 10 |    | *****************  |
|    | CD | GIVFILSGLCSMTGCSLYANKITTEFFDPLFVEQKYELGAALFIGWAGASLCIIGGVIFC |
|    |    |  |
|    | НР | FSISDNNKTPRYTYNGATSVMSSRTKYHGGEDFKTTNPSKQFDKNAYV             |
|    |    | **********   |
| 15 | CD | FSISDNNKTPRYTYNGATSVMSSRTKYHGGEDFKTTNPSKQFDKNAYV             |
|    |    |  |

Furthermore, the search of the GenBank using the base sequences of the present cDNA has revealed the registration of sequences that shared a homology of 90% or more (for example, Accession No. N41613) among ESTs. However, since they are partial sequences, it can not be judged whether or not they encode the same protein as the protein of the present invention.

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Determination of the whole base sequence of the cDNA insert of clone HP03879 obtained from cDNA library of human kidney revealed the structure consisting of a 33-bp 5'-untranslated region, a 918-bp ORF, and a 651-bp 3'-untranslated region. The ORF encodes a protein consisting of 305 amino acid residues and there existed one putative transmembrane domain at the N-terminus. Figure 33 depicts the hydrophobicity/hydrophilicity profile, obtained by the Kyte-Doolittle method, of the present protein. In vitro translation resulted in formation of a translation product of 34 kDa that was almost identical with the molecular weight of 34,073 predicted from the ORF.

The search of the protein database using the amino acid sequence of the present protein revealed that the protein was similar to human NADH-cytochrome b5 reductase (Accession No. Y09501). Table 23 shows the comparison between amino acid sequences of the human protein of the present invention (HP) and human NADH-cytochrome reductase (CT). Therein, the marks of -, \*, and . represent a gap, an amino acid residue identical with that of the protein of the present invention, and an amino acid residue similar to that of the protein of the present invention, respectively. The both proteins shared a homology of 63.5% in the entire region other than the N-terminal region.

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Table 23

|    | HP | MGIQTSPVLLASLGVGLVTLLGLAVGSYLVRRSRRPQVTLLDPNEKYLLRLLDKTTVSHN |
|----|----|--|
|    |    | * . ** * ** . ** ***. * **.                                  |
| 5  | CT | MGAQLSTLGHMVLFPVWFLYSLLMKLFQRS-TPAITLESPDIKYPLRLIDREIISHD    |
|    | HP | TKRFRFALPTAHHTLGLPVGKHIYLSTRIDGSLVIRPYTPVTSDEDQGYVDLVIKVYLKG |
|    |    | *. ******* *. ******. *****. *****. **. **. **. *.           |
|    | CT | TRRFRFALPSPQHILGLPVGQHIYLSARIDGNLVVRPYTPISSDDDKGFVDLVIKVYFKD |
| 10 |    |  |
|    | HP | VHPKFPEGGKMSQYLDSLKVGDVVEFRGPSGLLTYTGKGHFNIQPNKKSPPEPRVAKKLG |
|    |    | . *****. *******. * ** *******. * ***. *.                    |
|    | CT | THPKFPAGGKMSQYLESMQIGDTIEFRGPSGLLVYQGKGKFAIRPDKKSNPIIRTVKSVG |
|    |    |  |
| 15 | HP | MIAGGTGITPMLQLIRAILKVPEDPTQCFLLFANQTEKDIILREDLEELQARYPNRFKLW |
|    |    | ********************************                             |
|    | CT | MIAGGTGITPMLQVIRAIMKDPDDHTVCHLLFANQTEKDILLRPELEELRNKHSARFKLW |
|    |    |  |
|    | HP | FTLDHPPKDWAYSKGFVTADMIREHLPAPGDDVLVLLCGPPPMVQLACHPNLDKLGYSQK |
| 20 |    | . *** *. *. * *** ***. ***. * ** *                           |
|    | СТ | YTLDRAPEAWDYGQGFVNEEMIRDHLPPPEEEPLVLMCGPPPMIQYACLPNLDHVGHPTE |
|    |    |  |
|    | HP | MRFTY  |
|    |    | . *  |
| 25 | СТ | RCFVF  |

The search of the GenBank using the base sequences of the present cDNA has revealed the registration of sequences that shared a homology of 90% or more (for example, Accession No. F06459) among ESTs. However, since they are partial sequences, it can not be judged whether or not they encode the same protein as the protein of the present invention.

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<HP03880> (SEQ ID NOS: 94, 104 and 114)

Determination of the whole base sequence of the cDNA insert of clone HP03880 obtained from cDNA library of human kidney revealed the structure consisting of a 98-bp 5'-untranslated region, a 684-bp ORF, and a 115-bp 3'untranslated region. The ORF encodes a protein consisting of 15 amino acid residues and there existed a putative 227 secretory signal at the N-terminus. Figure 34 depicts the hydrophobicity/hydrophilicity profile, obtained by the Kyte-Doolittle method, of the present protein. translation resulted in formation of a translation product 20 of 28 kDa that was somewhat larger than the molecular weight of 25,717 predicted from the ORF. In this case, the addition of a microsome led to the formation of a product of 27 kDa. Application of the (-3,-1) rule, a method for predicting the cleavage site of the secretory signal sequence, allows to 25

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expect that the mature protein starts from aspartic acid at position 23.

The search of the protein database using the amino acid sequence of the present protein revealed that the protein was similar to rat phosphatidylethanolamine-binding protein (Accession No. P31044). Table 24 shows comparison between amino acid sequences of the human protein of the invention present (HP) and rat phosphatidylethanolamine-binding protein (RN). Therein, the marks of -, \*, and . represent a gap, an amino acid residue identical with that of the protein of the present invention, and an amino acid residue similar to that of the protein of the present invention, respectively. The both proteins shared a homology of 37.6% in the region of 133 amino acid residues other than the N-terminal region.

Table 24

HP MGWTMRLVTAALLLGLMMVVTGDEDENSPCAHEALLDEDTLFCQGLEVFYPELGNIGCKV

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RN

MAADISQWAGPLSLQEVDEPPQHALRVDYGGVTV

HP VPDCNNYRQKITSWMEPIVKFPGAVDGATYILVMVDPDAPSRAEPRQRFWRHWLVTDIKG

... \* \* \*.\*\*..\*\*\*\*\* .\*. \* \*.\*.\*\*

RN DELGKVLTPTQVMNRPSSISWDGLDPGKLYTLVLTDPDAPSRKDPKFREWHHFLVVNMKG

HP ADLKKGKIQGQELSAYQAPSPPAHSGFHRYQFFVYLQEGKV---ISLLP-KENKTRGSWK

\*\*. \*. \*\*. \*\*. \*\*\* .. \*\* .. \*\*

RN NDISSGTV----LSEYVGSGPPKDTGLHRYVWLVYEQEQPLNCDEPILSNKSGDNRGKFK

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HP MDRFLNRFHLGEPEASTQFMTQNYQDSPTLQAPRERASEPKHKNQAEIAAC

...\* ... \*\*\*. \* \* \* \* . . . . \*. \*.

RN VESFRKKYHLGAPVAGTCFQAEWDDSVPKLHDQLAGK

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The search of the GenBank using the base sequences of the present cDNA has revealed the registration of sequences that shared a homology of 90% or more (for example, Accession No. H83784) among ESTs. However, since they are partial sequences, it can not be judged whether or not they encode the same protein as the protein of the present invention.

<HP10704> (SEQ ID NOS: 95, 105 and 115)

Determination of the whole base sequence of the

CDNA insert of clone HP10704 obtained from cDNA library of
human kidney revealed the structure consisting of a 141-bp
5'-untranslated region, a 1326-bp ORF, and a 399-bp 3'untranslated region. The ORF encodes a protein consisting of
441 amino acid residues and there existed eight putative
transmembrane domains. Figure 35 depicts the

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hydrophobicity/hydrophilicity profile, obtained by the Kyte-Doolittle method, of the present protein. In vitro translation resulted in formation of a translation product of high molecular weight.

The search of the protein database using the amino acid sequence of the present protein revealed that the protein was similar to human unknown gene product (Accession No. AAC27544). Table 25 shows the comparison between amino acid sequences of the human protein of the present invention (HP) and human unknown gene product (UP). Therein, the marks of -, \*, and . represent a gap, an amino acid residue identical with that of the protein of the present invention, and an amino acid residue similar to that of the protein of the present invention, respectively. The both proteins shared a homology of 39.1% in the entire region.

Table 25

HP MAIHKALVMCLGLPLFLFPG-AWAQGHVPPGCSQGLNPLYYNLCDRSGAWGIVLE

\* \*\*... \* ... \*\* \* \* .\*\*\* .. \*\*\*\*.\*

UN MFVASERKMRAHQVLTFLLLFVITSVASENASTSRGCGLDLLPQYVSLCDLDAIWGIVVE

UN AVAGAGALITLLLMLILLVRLPFIKEKEKKSPVGLHFLFLLGTLGLFGLTFAFIIQEDET

|    | HP | TCASRRFLFGVLFAICFSCLAAHVFALNFLARKNHGPRGWVIFTVALLLTLVEVIINTEW |
|----|----|--|
|    |    | ·*· ****·********** · · · · · * · * ** · · · · ** * ** · **  |
|    | UN | ICSVRRFLWGVLFALCFSCLLSQAWRVRRLVRHGTGPAGWQLVGLALCLMLVQVIIAVEW |
| 5  |    |  |
|    | HP | LIITLVRGSGEGGPQGNSSAGWAVASPCAIANMDFVMALIYVMLLLLGAFLGAWPALCGR |
|    |    | *** *** . ******* *.** * .***.                               |
|    | UN | LVLTVLRDTRPACAYEPMDFVMALIYDMVLLVVTLGLALFTLCGK                |
|    |    |  |
| 10 | HP | YKRWRKHGVFVLLTTATSVAIWVVWIVMYTYGN-KQHNSPTWDDPTLAIALAANAWAFVL |
|    |    | · ***. · *. *. *. ** ***. ** · · · · · ·                     |
|    | UN | FKRWKLNGAFLLITAFLSVLIWVAWMTMYLFGNVKLQQGDAWNDPTLAITLAASGWVFVI |
|    |    | •  |
|    | HP | FYVIPEVSQVTKSSPEQSYQGDMYPTRGVGY-ETILKEQ-KGQSMFVENKAFSMDEPVAA |
| 15 |    | **** * *   |
|    | UN | FHAIPEI-HCTLLPALQENTPNYFDTSQPRMRETAFEEDVQLPRAYMENKAFSMDEHNAA |
|    |    |  |
|    | НР | KRPVS-PYSGYNGQLLTSVYQPTEMALMHKVPSEGAYDIILPRATANSQVMGSANSTLRA |
|    |    | * *  |
| 20 | UN | LRTAGFPNGSLGKRPSGSLGKRPSAPFRSNVYQPTEMAVVLNGGTIPTAPPSHTGRHLW  |
|    |    |  |
|    | HP | EDMYSAQSHQAATPPKDGKNSQVFRNPYVWD                              |
|    |    |  |

of the present cDNA has revealed the registration of sequences that shared a homology of 90% or more (for example, Accession No. AA346702) among ESTs. However, since they are partial sequences, it can not be judged whether or not they encode the same protein as the protein of the present invention.

<HP10715> (SEQ ID NOS: 96, 106 and 116)

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Determination of the whole base sequence of the cDNA insert of clone HP10715 obtained from cDNA library of human umbilical cord blood revealed the structure consisting of a 49-bp 5'-untranslated region, a 798-bp ORF, and a 1351-3'-untranslated region. The ORF encodes a protein consisting of 265 amino acid residues and there existed two putative transmembrane domains. Figure 36 depicts the hydrophobicity/hydrophilicity profile, obtained by the Kyte-Doolittle method, of present protein. the In vitro translation resulted in formation of a translation product of 43 kDa that was larger than the molecular weight of 29,217 predicted from the ORF.

The search of the GenBank using the base sequences of the present cDNA has revealed the registration of sequences that shared a homology of 90% or more (for example, Accession No. AI381750) among ESTs. However, since they are partial sequences, it can not be judged whether or not they encode the same protein as the protein of the present

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<HP10724> (SEQ ID NOS: 97, 107 and 117)

Determination of the whole base sequence of the cDNA insert of clone HP10724 obtained from cDNA library of human umbilical cord blood revealed the structure consisting of a 68-bp 5'-untranslated region, a 627-bp ORF, and a 1485-bp 3'-untranslated region. The ORF encodes a protein consisting of 208 amino acid residues and there existed one putative transmembrane domain at the N-terminus. Figure 37 depicts the hydrophobicity/hydrophilicity profile, obtained by the Kyte-Doolittle method, of the present protein. In vitro translation resulted in formation of a translation product of 24 kDa that was almost identical with the molecular weight of 23,850 predicted from the ORF.

The search of the GenBank using the base sequences of the present cDNA has revealed the registration of sequences that shared a homology of 90% or more (for example, Accession No. T78035) among ESTs. However, since they are partial sequences, it can not be judged whether or not they encode the same protein as the protein of the present invention.

<HP10733> (SEQ ID NOS: 98, 108 and 118)

Determination of the whole base sequence of the cDNA insert of clone HP10733 obtained from cDNA library of human umbilical cord blood revealed the structure consisting

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of a 102-bp 5'-untranslated region, a 1203-bp ORF, and a 222-bp 3'-untranslated region. The ORF encodes a protein consisting of 400 amino acid residues and there existed a putative secretory signal at the N-terminus and one putative transmembrane domain in the inner portion. Figure 38 depicts the hydrophobicity/hydrophilicity profile, obtained by the Kyte-Doolittle method, of the present protein. In vitro translation resulted in formation of a translation product of 50 kDa that was larger than the molecular weight of 43,151 predicted from the ORF. In this case, the addition of a microsome led to the formation of a product of 54 kDa. In addition, there exist in the amino acid sequence of this protein four sites at which N-glycosylation may occur (Asn-Leu-Thr at position 52, Asn-Ala-Ser at position 131, Asn-Ile-Thr at position 145 and Asn-Leu-Ser at position 343). Application of the (-3,-1) rule, a method for predicting the cleavage site of the secretory signal sequence, allows to expect that the mature protein starts from arginine at position 33.

The search of the protein database using the amino acid sequence of the present protein revealed that the protein was similar to Drosophila melanogaster GOLIATH protein (Accession No. Q06003). Table 26 shows the comparison between amino acid sequences of the human protein of the present invention (HP) and Drosophila melanogaster

GOLIATH protein (DM). Therein, the marks of -, \*, and . represent a gap, an amino acid residue identical with that of the protein of the present invention, and an amino acid residue similar to that of the protein of the present invention, respectively. The both proteins shared a homology of 35.0% in the entire region.

Table 26

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10 HP MAWRREASVGARGVLALALLALALCVPGARGRALEWFSAVVNIEYVDPQTNLTVWSVSE

 $HP \ \ SGRFGDSSPKEGAHGLVGVPWAPGGDLEGCAPDTRFFVPEPGGRGAAPWVALVARGGCTF$ 

HP KDKVLVAARRNASAVVLYNEERYGNITLPMSHAGTGNIVVIMISYPKGREILEL-VQKGI

\* \*....\*\*.

DM MQLEKMQIKGKTRNIAAVITYQNIGQDLSLTLDKGY

HP PVTMTIGVGTRHVQEF--ISGQSVVFVAIAFITMMIISLAWLIFYYIQRFLY-TGSQIGS

\*\*. \* \* \* \* \*. . . \*\*. \*\*. \* \* \*\*\*\*\*\*\* \* . . . \*

DM NVTISIIEGRRGVRTISSLNRTSVLFVSISFI--VDDILCWLIFYYIQRFRYMQAKDQQS

HP QSHRKETKKVIGQLLLHTVKHGEKGIDVDAENCAVCIENFKVKDIIRILPCKHIFHRICI

DM RNLCSYTKKAIMKIPTKTGKFSD-EKDLDSDCCAICIEAYKPTDTIRILPCKHEFHKNCI

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|   | HP | DPWLLDHRTCPMCKLDVIKALGYWGEPGDVQEMPAPESPPGRDPAANLSLALPDDDGSDE |
|---|----|--|
|   |    | ****. ********* **   |
|   | DM | DPWLIEHRTCPMCKLDVLKFYGY-VVGDQIYQTPSPQHTAPIASIEEVPVIVVAVPHGPQ |
|   |    |  |
| 5 | HP | SSPPSASPAESEPQCDPSFKGDAGENTALLEAGRSDSRHGGPIS                 |
|   |    | * * *  |
|   | DM | PLQPLQASNMSSFAPSHYFQSSRSPSSSVQQQLAPLTYQPHPQQAASERGRRNSAPATMP |
|   |    |  |

The search of the GenBank using the base sequences of the present cDNA has revealed the registration of sequences that shared a homology of 90% or more (for example, Accession No. AI286184) among ESTs. However, since they are partial sequences, it can not be judged whether or not they encode the same protein as the protein of the present invention.

<HP10734> (SEQ ID NOS: 99, 109 and 119)

Determination of the whole base sequence of the cDNA insert of clone HP10734 obtained from cDNA library of human umbilical cord blood revealed the structure consisting of a 124-bp 5'-untranslated region, a 579-bp ORF, and a 1202-bp 3'-untranslated region. The ORF encodes a protein consisting of 192 amino acid residues and there existed one putative transmembrane domain. Figure 39 depicts the hydrophobicity/hydrophilicity profile, obtained by the Kyte-

Doolittle method, of the present protein. In vitro translation resulted in formation of a translation product of high molecular weight.

The search of the protein database using the amino

acid sequence of the present protein revealed that the
protein was similar to human sodium channel ß2 subunit
(Accession No. AAD47196). Table 27 shows the comparison
between amino acid sequences of the human protein of the
present invention (HP) and human sodium channel ß2 subunit

(SC). Therein, the marks of -, \*, and . represent a gap, an
amino acid residue identical with that of the protein of the
present invention, and an amino acid residue similar to that
of the protein of the present invention, respectively. The
both proteins shared a homology of 26.3% in the N-terminal
region of 152 amino acid residues.

Table 27

HP CIFKIDWTLSPGEHAKDE-YVLYYYSNLSVPIGRFQNRVHLMGDNLCNDGSLLLQDVQEA

\*...\*\* ....\* .... \*\*...\*. . \* \*...\*\*.

SC KQFSLNWTYQECNNCSEEMFLQFRMKIINLKLERFQDRVEFSGNPSKYDVSVMLRNVQPE

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HP DQGTYICEIRLKGESQVFKKAVVLHVLPEEPKELMVHVGGLIQMGCVFQSTEVKHVTKVE

SC DEGIYNCYIMNPPDRHRGHGKIHLQVLMEEPPERDFTVAVIVGASVGGFLAVVILVLMVV

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HP WIFSGRRAKVTRRKHHCVREGSG

SC KCVRRKKEQKLSTDDLKTEEEGKTDGEGNPDDGAK

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The search of the GenBank using the base sequences of the present cDNA has revealed the registration of sequences that shared a homology of 90% or more (for example, Accession No. C03216) among ESTs. However, since they are partial sequences, it can not be judged whether or not they encode the same protein as the protein of the present invention.

<HP10756> (SEQ ID NOS: 100, 110 and 120)

cDNA insert of clone HP10756 obtained from cDNA library of human kidney revealed the structure consisting of a 49-bp 5'-untranslated region, a 783-bp ORF, and a 166-bp 3'-untranslated region. The ORF encodes a protein consisting of 260 amino acid residues and there existed a putative secretory signal at the N-terminus. Figure 40 depicts the

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hydrophobicity/hydrophilicity profile, obtained by the Kyte-Doolittle method, of the present protein. In vitro translation resulted in formation of a translation product of 27 kDa that was almost identical with the molecular weight of 27,356 predicted from the ORF.

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Furthermore, the search of the GenBank using the base sequences of the present cDNA has revealed the registration of sequences that shared a homology of 90% or more (for example, Accession No. AW027769) among ESTs. However, since they are partial sequences, it can not be judged whether or not they encode the same protein as the protein of the present invention.

<HP03670> (SEQ ID NOS: 121, 131 and 141)

Determination of the whole base sequence of the cDNA insert of clone HP03670 obtained from cDNA library of human umbilical cord blood revealed the structure consisting of a 77-bp 5'-untranslated region, a 1014-bp ORF, and a 531-bp 3'-untranslated region. The ORF encodes a protein consisting of 337 amino acid residues and there existed at least seven putative transmembrane domains. Figure 41 depicts the hydrophobicity/hydrophilicity profile, obtained by the Kyte-Doolittle method, of the present protein.

The search of the protein database using the amino acid sequence of the present protein revealed that the protein was similar to human hypothetical protein KIAA0260

(Accession No. BAA13390). Table 28 shows the comparison between amino acid sequences of the human protein of the present invention (HP) and human hypothetical protein KIAA0260 (KI). Therein, the marks of -, \*, and . represent a gap, an amino acid residue identical with that of the protein of the present invention, and an amino acid residue similar to that of the protein of the present invention, respectively. The both proteins shared a homology of 57.6% in the entire region other than the N-terminal region. In addition, the C-terminal region beginning from leucine at position 77 matched with human putative Sqv-7-like protein (Accession No. AJ005866) except one amino acid residue.

Table 28

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HP

MTAGGQAEAEGAGGEPG

- KI NSWSPLGAAAAGPRAARPRRQATAAAAAMAEVHRRQHARVKGEAPAKSSTLRDEEELGMA

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| ΚT | LRVVKFPDLD | RNVPRKTFPL | PLLYFGNQITGI | FSTKKLNL | .PMFTVLR | RFSILF | TMFAEGV |
|----|------------|------------|--------------|----------|----------|--------|---------|
|----|------------|------------|--------------|----------|----------|--------|---------|

HP ILGKQYSLNIILSVFAIILGAFIAAGSDLAFNLEGYIFVFLNDIFTAANGVYTKQKMDPK 

KI LLKKTFSWGIKMTVFAMIIGAFVAASSDLAFDLEGYAFILINDVLTAANGAYVKQKLDSK

- HP ELGKYGVLFYNACFMIIPTLIISVSTGDLQQATEFNQWKNVVFILQFLLSCFLGFLLMYS KI ELGKYGLLYYNALFMILPTLAIAYFTGDAQKAVEFEGWADTLFLLQFTLSCVMGFILMYA
- HP TVLCSYYNSALTTAVVGAIKNVSVAYIGILIGGDYIFSLLNFVGLNICMAGGLRYSFLTL \*\*\*\*. \*\*\*\*\*\*. \*\* \*\*\*. . . \*\*\*. . . \*\*\*\*. \*\*. \*\*. \*\*. \*\*. \*\*. \*\*. \* KI TVLCTQYNSALTTTIVGCIKNILITYIGMVFGGDYIFTWTNFIGLNISIAGSLVYSYITF
- HP SSQLKPKPVGEENICLDLKS 15 ... .\*. .\*. \*\*.\*. KI TEEQLSKQ-SEANNKLDIKGKGAV

The search of the GenBank using the base sequences of the present cDNA has revealed the registration of sequences that shared a homology of 90% or more (for example, Accession No. R24922) among ESTs. However, since they are partial sequences, it can not be judged whether or not they encode the same protein as the protein of the present 25

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<HP03688> (SEQ ID NOS: 122, 132 and 142)

Determination of the whole base sequence of the cDNA insert of clone HP03688 obtained from cDNA library of human umbilical cord blood revealed the structure consisting of a 35-bp 5'-untranslated region, a 711-bp ORF, and a 1729bp 3'-untranslated region. The ORF encodes a protein consisting of 236 amino acid residues and there existed five putative transmembrane domains. Figure 42 depicts hydrophobicity/hydrophilicity profile, obtained by the Kyte-Doolittle method, of present protein. the translation resulted in formation of a translation product of high molecular weight.

The search of the protein database using the amino

acid sequence of the present protein revealed that the
protein was similar to Caenorhabditis elegans hypothetical
protein W02D9 (Accession No. CAB03470). Table 29 shows the
comparison between amino acid sequences of the human protein
of the present invention (HP) and Caenorhabditis elegans

hypothetical protein W02D9 (CE). Therein, the marks of -, \*,
and . represent a gap, an amino acid residue identical with
that of the protein of the present invention, and an amino
acid residue similar to that of the protein of the present
invention, respectively. The both proteins shared a homology
of 50.8% in the entire region other than the N-terminal

| m - | able 29   |
|-----|---|
| 10  | ADIE 29   |
| HF  | MAEAE   |
| CE  | E MEILNLSSKFSLSDKPCQKFIFSLFSAVQNSRFKIISFPEIHQKPLPQEEMNSFGNASV   |
| HI  | P SPGDPGTASPRPLFAGLSDISISQDIPVEGEITIPMRSRIREFDSSTLNESVRNTIMRD   |
|     | ** **. *. **. **. **.   |
| Cl  | E IDMLEQEMAAEQTANLSGNIAGMSAPKSSSNRRGPMQEVDLDAEFDTLEEPVWDTVKRD   |
|     |   |
| H   | P KAVGKKFMHVLYPR-KSNTLLRDWDLWGPLILCVTLALMLQRDSADSEKDGGPQFAEVF   |
|     | . ** ** **. * ********* **. **.   |
| С   | E LTVGAKFTHVVLPHGDKQQLLRDWDLWGPLFICVGLALLLQHNGGTESAPQFTQVF  |
| Н   | P IVWFGAVTITLNSKLLGGNISFFQSLCVLGYCILPLTVAMLICRLVLLADPGPVNFMVI   |
|     | ***.*.* * **************************  |
| C   | E ITFFGSVIVTANIKLLGGNISFFQSLCVIGYCLLPPFVAAVLCSL-FLHGIAFPL   |
|     |   |
| ŀ   | IP FVVIVMFAWSIVASTAFLADSQPPNRRALAVYPVFLFYFVISWMILTFTPQ  |
|     | ··· · * <sub>·</sub> ** <sub>·</sub> ** · *** <sub>·</sub> · ** · · * * <sub>·</sub> · ******* <sub>·</sub> **** <sub>·</sub> . |
| (   | CE LITSIGFVWSTYASMGFLAGCQPDKKRLLVIYPVFLFYFVVSWMIISHS  |

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Furthermore, the search of the GenBank using the base sequences of the present cDNA has revealed the registration of sequences that shared a homology of 90% or more (for example, Accession No. T51465) among ESTs. However, since they are partial sequences, it can not be judged whether or not they encode the same protein as the protein of the present invention.

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<HP03825> (SEQ ID NOS: 123, 133 and 143)

Determination of the whole base sequence of the cDNA insert of clone HP03825 obtained from cDNA library of human kidney revealed the structure consisting of a 20-bp 5'-untranslated region, a 1683-bp ORF, and a 36-bp 3'untranslated region. The ORF encodes a protein consisting of 560 amino acid residues and there existed seven putative transmembrane domains. Figure 43. depicts the hydrophobicity/hydrophilicity profile, obtained by the Kytepresent protein. Doolittle method, of the translation resulted in formation of a translation product of 56 kDa that was smaller than the molecular weight of 64,047 predicted from the ORF.

The search of the protein database using the amino acid sequence of the present protein revealed that the protein was similar to Mycobacterium tuberculosis hypothetical protein Rv0235c (Accession No. CAB07001).

Table 30 shows the comparison between amino acid sequences

of the human protein of the present invention (HP) and Mycobacterium tuberculosis hypothetical protein Rv0235c (MT). Therein, the marks of -, \*, and . represent a gap, an amino acid residue identical with that of the protein of the present invention, and an amino acid residue similar to that of the protein of the present invention, respectively. The both proteins shared a homology of 41.7% in the entire region other than the N-terminal region. In addition, the region from alanine at position 293 to proline at position 502 matched with human putative novel protein c360B4.1 (Accession No. CAB56180).

Table 30

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HP MAAPAESLRRRKTGYSDPEPESPPAPGRGPAGSPAHLHTGTFWLTRIVLLKALAFVYFVA
...\*\*.\*..\*..\*

MT MGWFSAPEYWLGRLALERGTAIIYLIA

HP LLALLGLGISSFVLITGCANMLLMAALWGLYMSLVNVGHVWYSFGWESQLLETGFLGIFL

\* . \* . \*\*\* . \*. \*\* \*\* . \*\*\*\*\*\* \*\*\*

MT --AAVVAGAASFVPLW--ATMLIWLTLWVLYLSIVNVGQAWYSFGWESLLLETGFLMIFL

|    | HP | CPLWTLSRLPQHTPTSR1VLWGFRWL1FR1MLGAGL1K1RGDRCWRDLTCMDFHYETQPM |
|----|----|--|
|    |    | .* .**. ***.**. ****.***.****. ****                          |
|    | MT | GNERTAPPILTLLLA-RWLLFRVEFGAGLIKMRGDSCWRSLTCLYYHHETQPM        |
| 5  |    |  |
|    | HP | PNPVAYYLHHSPWWFHRFETLSNHFIELLVPFFLFLGRRACIIHGVLQILFQAVLIVSGN |
|    |    | *. * ** * ** * * *   |
|    | MT | PGPLSWFFHHLPKPLHRIEVAGNHFAQLVVPFGLFTPQPAASIAAAIIVVTQLWLVASGN |
|    |    |  |
| 10 | HP | LSFLNWLTMVPSLACFDDATLGFLFPSGPGSLKDRVLQMQRDIRGARPEPRFGSVVRRAA |
|    |    | .*.**** ********   |
|    | MT | FSWLNWLTILLACSAIDTSS-AAALLPMPAQPALSAPPQWFAGLVV               |
|    |    |  |
|    | HP | NVSLGVLLAWLSVPVVLNLLSSRQVMNTHFNSLHIVNTYGAFGSITKERAEVILQGTASS |
| 15 |    | *** ** . *****. * ** ** * ****** * ** *                      |
|    | MT | VFTAAVLLLSYWPARNLLSSHQRMNMSFNPFHLVNTYGAFGSICRTRREVVIEGTDES   |
|    |    |  |
|    | HP | NASAPDAMWEDYEFKCKPGDPSRRPCLISPYHYRLDWLMWFAAFQTYEHNDWIIHLAGKL |
|    |    | * . * * * * * * * * * * * * * *                              |
| 20 | MT | -PITEQTVWKAYEFKGKPGDPRRLPRQWAPYHLRLDWLMWFAAISPGYALPWMTPFLNRL |
|    |    |  |
|    | HP | LASDAEALSLLAHNPFAGRPPPRWVRGEHYRYKFSRPGGRHAAEGKWWVRKRIGAYFPPL |
|    |    | * . * * . * * * * * *  |
|    | MT | LRNDPATLKLLRHNPFP-QSPPRYVRAQLYQYRFTTVAELRRDRA-WWHRTLIGRYVPPM |

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HP SLEELRPYFRDRGWPLPGPL

\*\* ..

MT SLRKVASPPAD

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The search of the GenBank using the base sequences of the present cDNA has revealed the registration of sequences that shared a homology of 90% or more (for example, Accession No. AA019047) among ESTs. However, since they are partial sequences, it can not be judged whether or not they encode the same protein as the protein of the present invention.

<HP03877> (SEQ ID NOS: 124, 134 and 144)

Determination of the whole base sequence of the 15 cDNA insert of clone HP03877 obtained from cDNA library of human kidney revealed the structure consisting of a 106-bp 5'-untranslated region, a 1221-bp ORF, and a 678-bp 3'untranslated region. The ORF encodes a protein consisting of 406 amino acid residues and there existed four putative 20 transmembrane domains. Figure 44 depicts the hydrophobicity/hydrophilicity profile, obtained by the Kyte-Doolittle method, of the present protein. In vitro translation resulted in formation of a translation product of 49 kDa that was somewhat larger than the molecular weight 25 of 46,208 predicted from the ORF.

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The search of the protein database using the amino acid sequence of the present protein revealed that the protein was similar to Caenorhabditis elegans hypothetical protein Y37D8A (Accession No. CAA21543). Table 31 shows the comparison between amino acid sequences of the human protein of the present invention (HP) and Caenorhabditis elegans hypothetical protein Y37D8A (CE). Therein, the marks of -, \*, and . represent a gap, an amino acid residue identical with that of the protein of the present invention, and an amino acid residue similar to that of the protein of the present invention, respectively. The both proteins shared a homology of 50.2% in the intermediate region of 329 amino acid residues.

15 Table 31

HP

MAENG

CE MAKKQKKSTEKSERTVEFKEPPKPANSEERLVSTRQFLAKIGQKKLIKKKVKNFRFSKKT

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HP KNCDQRRVAMNKEHHNGNFTDPSSVNEKKRREREERQNIVLWRQPLITLQYFSLEILVIL

.\* \*\*..\*\*.\* \*...\* .\*\*

CE FIDFFSENQKKNCRLKPAGRGMKPSPSQNTLNRMERETIVFWRRPHIVIPYALMEIAHLA

25 HP KEWTSKLWHRQSIVVSFLLLLAVLIATYYVEGVHQQYVQRIEKQFLLYAYWIGLGILSSV

|    | * * * . * . * * * * * * * * . * * * * *  |
|----|--|
|    | CE VELFFKILAHKTVLLLTAISIGLAVYGYHAPGAHQEHVQTIEKHILWWSWWVLLGVLSSI  |
|    | HP GLGTGLHTFLLYLGPHIASVTLAAYECNSVNFPEPPYPDQIICPDEEGTEGTISLWSIIS  |
| 5  | ***. ******. *******. **. **. ***. * ** * *  CE GLGSGLHTFLIYLGPHIAAVTMAAYECQSLDFPQPPYPESIQCPSTKSSI-AVTFWQIVA |
|    | HP KVRIEACMWGIGTAIGELPPYFMARAARLSGAEPDDEEYQEFEEMLEHAESAQDFA-   |
| 10 | ***. *. ** ***. *********** **. **. ** *   |
|    | HP -SRAKLAVQKLVQKVGFFGILACASIPNPLFDLAGITCGHFLVPFWTFFGATLIGKAIIK  |
|    | . *** *** *** *******************  |
| 15 |  |
|    | HP MHIQKIFVIITFSKHIVEQMVAFIGAVPGIGPSLQKPFQEYLEAQRQKLHHKSEMGTPQG  **.*. ***. **. *                            |
|    | CE MHVQMGFVILAFSDHHAENFVKILEKIPAVGPYIRQPISDLLEKQRKALHKTPGEHSEQD  |
| 20 | HP ENWLSWMFEKLVVVMVCYFILSIINSMAQSYAKRIQQRLNSEEKTK  |
|    | CE LIDEENQSFEEEEEEAVTPPSSCPLLLSDGFEGVVVKK  |

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of the present cDNA has revealed the registration of sequences that shared a homology of 90% or more (for example, Accession No. T18977) among ESTs. However, since they are partial sequences, it can not be judged whether or not they encode the same protein as the protein of the present invention.

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<HP10765> (SEQ ID NOS: 125, 135 and 145)

Determination of the whole base sequence of the cDNA insert of clone HP10765 obtained from cDNA library of human umbilical cord blood revealed the structure consisting of a 30-bp 5'-untranslated region, a 1362-bp ORF, and a 166-bp 3'-untranslated region. The ORF encodes a protein consisting of 453 amino acid residues and there existed a putative secretory signal at the N-terminus and one putative transmembrane domain in the inner portion. Figure 45 depicts the hydrophobicity/hydrophilicity profile, obtained by the Kyte-Doolittle method, of the present protein. In vitro translation resulted in formation of a translation product of 48 kDa that was almost identical with the molecular weight of 47,724 predicted from the ORF.

The search of the GenBank using the base sequences of the present cDNA has revealed the registration of sequences that shared a homology of 90% or more (for example, Accession No. AI792834) among ESTs. However, since they are partial sequences, it can not be judged whether or not they

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encode the same protein as the protein of the present invention.

<HP10766> (SEQ ID NOS: 126, 136 and 146)

Determination of the whole base sequence of the 5 cDNA insert of clone HP10766 obtained from cDNA library of human kidney revealed the structure consisting of a 150-bp 5'-untranslated region, a 180-bp ORF, and a 675-bp 3'untranslated region. The ORF encodes a protein consisting of amino acid residues and there existed two putative 10 transmembrane domains. Figure 46 depicts the hydrophobicity/hydrophilicity profile, obtained by the Kyte-Doolittle method, of the present protein. In vitro translation resulted in formation of a translation product kDa or less that was almost identical with the 15 molecular weight of 6,098 predicted from the ORF.

The search of the GenBank using the base sequences of the present cDNA has revealed the registration of sequences that shared a homology of 90% or more (for example, Accession No. T85491) among ESTs. However, since they are partial sequences, it can not be judged whether or not they encode the same protein as the protein of the present invention.

<HP10770> (SEQ ID NOS: 127, 137 and 147)

Determination of the whole base sequence of the cDNA insert of clone HP10770 obtained from cDNA library of

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human kidney revealed the structure consisting of a 150-bp 5'-untranslated region, a 633-bp ORF, and a 186-bp 3'-untranslated region. The ORF encodes a protein consisting of 210 amino acid residues and there existed two putative transmembrane domains. Figure 47 depicts the hydrophobicity/hydrophilicity profile, obtained by the Kyte-Doolittle method, of the present protein. In vitro translation resulted in formation of a translation product of 27 kDa that was larger than the molecular weight of 22,156 predicted from the ORF.

The search of the GenBank using the base sequences of the present cDNA has revealed the registration of sequences that shared a homology of 90% or more (for example, Accession No. AI792771) among ESTs. However, since they are partial sequences, it can not be judged whether or not they encode the same protein as the protein of the present invention.

<HP10772> (SEQ ID NOS: 128, 138 and 148)

cDNA insert of clone HP10772 obtained from cDNA library of human kidney revealed the structure consisting of a 19-bp 5'-untranslated region, a 498-bp ORF, and a 724-bp 3'-untranslated region. The ORF encodes a protein consisting of 165 amino acid residues and there existed four putative transmembrane domains. Figure 48 depicts the

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hydrophobicity/hydrophilicity profile, obtained by the Kyte-Doolittle method, of the present protein. In vitro translation resulted in formation of a translation product of high molecular weight.

The search of the GenBank using the base sequences of the present cDNA has revealed the registration of sequences that shared a homology of 90% or more (for example, Accession No. F11871) among ESTs. However, since they are partial sequences, it can not be judged whether or not they encode the same protein as the protein of the present invention.

<HP10773> (SEQ ID NOS: 129, 139 and 149)

Determination of the whole base sequence of the cDNA insert of clone HP10773 obtained from cDNA library of human kidney revealed the structure consisting of a 186-bp 5'-untranslated region, a 489-bp ORF, and a 499-bp 3'untranslated region. The ORF encodes a protein consisting of 162 amino acid residues and there existed four putative transmembrane domains. Figure 49 depicts hydrophobicity/hydrophilicity profile, obtained by the Kyte-Doolittle method, of the present protein. In vitro translation resulted in formation of a translation product of high molecular weight.

The search of the GenBank using the base sequences of the present cDNA has revealed the registration of

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sequences that shared a homology of 90% or more (for example, Accession No. N33828) among ESTs. However, since they are partial sequences, it can not be judged whether or not they encode the same protein as the protein of the present invention.

<HP10776> (SEQ ID NOS: 130, 140 and 150)

Determination of the whole base sequence of the cDNA insert of clone HP10776 obtained from cDNA library of human kidney revealed the structure consisting of a 207-bp 5'-untranslated region, a 666-bp ORF, and a 139-bp 3'untranslated region. The ORF encodes a protein consisting of 221 amino acid residues and there existed three putative transmembrane domains. Figure 50 depicts the hydrophobicity/hydrophilicity profile, obtained by the Kyte-Doolittle method, of the present protein. In translation resulted in formation of a translation product of 30 kDa that was larger than the molecular weight of 24,883 predicted from the ORF.

base sequences of the present cDNA has revealed the registration of sequences that shared a homology of 90% or more (for example, Accession No. AI929639) among ESTs. However, since they are partial sequences, it can not be judged whether or not they encode the same protein as the protein of the present invention.

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## INDUSTRIAL APPLICABILITY

The present invention provides human proteins having hydrophobic domains, DNAs encoding these proteins, expression vectors for these DNAs and eukaryotic cells expressing these DNAs. Since all of the proteins of the present invention are secreted or exist in the cell membrane, proteins controlling are considered to be proliferation and/or the differentiation of the cells. Accordingly, the proteins of the present invention can be employed as pharmaceuticals such as carcinostatic agents the proliferation and/or control to act differentiation of the cells, or as antigens for preparing antibodies against these proteins. The DNAs of the present invention can be utilized as probes for the 15 diagnosis and gene sources for the gene therapy. Furthermore, the DNAs can be utilized for expressing these proteins in into which these genes large quantities. Cells introduced to express these proteins can be utilized for corresponding receptors or the detection of 20 screening of novel small molecule pharmaceuticals and the like. The antibody of the present invention can be utilized for the detection, quantification, purification and the like of the protein of the present invention.

> provides invention also present The

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corresponding to the polynucleotide sequences disclosed herein. "Corresponding genes" are the regions of the genome that are transcribed to produce the mRNAs from which cDNA polynucleotide sequences are derived and may include contiguous regions of the genome necessary for the regulated expression of such genes. Corresponding genes may therefore include but are not limited to coding sequences, 5' and 3' untranslated regions, alternatively spliced exons, introns, promoters, enhancers, and silencer or suppressor elements. The corresponding genes can be isolated in accordance with known methods using the sequence information disclosed herein. Such methods include the preparation of probes or primers from the disclosed sequence information identification and/or amplification of genes in appropriate genomic libraries or other sources of genomic materials. An "isolated gene" is a gene that has been separated from the adjacent coding sequences, if any, present in the genome of the organism from which the gene was isolated.

Organisms that have enhanced, reduced, or modified 20 expression of the gene(s) corresponding to polynucleotide sequences disclosed herein are provided. The desired change in gene expression can be achieved through the use of antisense polynucleotides or ribozymes that bind and/or cleave the mRNA transcribed from the gene (Albert and Pharmacol. 25 Morris, 1994, Trends Sci. 15(7): 250-254;

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Lavarosky et al., 1997, Biochem. Mol. Med. 62(1): 11-22; and Hampel, 1998, Prog. Nucleic Acid Res. Mol. Biol. 58: 1-39; all of which are incorporated by reference herein). Transgenic animals that have multiple copies of the gene(s) corresponding to the polynucleotide sequences disclosed herein, preferably produced by transformation of cells with genetic constructs that are stably maintained within the are transformed cells and their progeny, provided. have modified genetic control Transgenic animals that regions that increase or reduce gene expression levels, or that change temporal or spatial patterns of gene expression, are also provided (see European Patent No. 0 649 464 B1, incorporated by reference herein). In addition, organisms are provided in which the gene(s) corresponding to the polynucleotide sequences disclosed herein have been partially or completely inactivated, through insertion of extraneous sequences into the corresponding gene(s) through deletion of all or part of the corresponding gene(s). Partial or complete gene inactivation can be accomplished through insertion, preferably followed by imprecise excision, of transposable elements (Plasterk, 1992, Bioessays 14(9): 629-633; Zwaal et al., 1993, Proc. Natl. Acad. Sci. USA 90(16): 7431-7435; Clark et al., 1994, Proc. Natl. Acad. Sci. USA 91(2): 719-722; all of which are incorporated by reference herein), or through homologous recombination,

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preferably detected by positive/negative genetic selection strategies (Mansour et al., 1988, Nature 336: 348-352; U.S. Patent Nos. 5,464,764; 5,487,992; 5,627,059; 5,631,153; 5,614, 396; 5,616,491; and 5,679,523; all of which are incorporated by reference herein). These organisms with altered gene expression are preferably eukaryotes and more preferably are mammals. Such organisms are useful for the development of non-human models for the study of disorders involving the corresponding gene(s), and for the development of assay systems for the identification of molecules that interact with the protein product(s) of the corresponding gene(s). Where the protein of the present invention is membrane-bound (e.g., is a receptor), the present invention also provides for soluble forms of such protein. In such forms part or all of the intracellular and transmembrane domains of the protein are deleted such that the protein is fully secreted from the cell in which it is expressed. The intracellular and transmembrane domains of proteins of the identified in accordance with known invention can be techniques for determination of such domains from sequence information.

Proteins and protein fragments of the present invention include proteins with amino acid sequence lengths that are at least 25% (more preferably at least 50%, and most preferably at least 75%) of the length of a disclosed

protein and have at least 60% sequence identity (more preferably, at least 75% identity; most preferably at least 90% or 95% identity) with that disclosed protein, where sequence identity is determined by comparing the amino acid sequences of the proteins when aligned so as to maximize overlap and identity while minimizing sequence gaps. Also included in the present invention are proteins and protein fragments that contain a segment preferably comprising 8 or more (more preferably 20 or more, most preferably 30 or more) contiguous amino acids that shares at least 75% sequence identity (more preferably, at least 85% identity; most preferably at least 95% identity) with any such segment of any of the disclosed proteins.

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Species homologs of the disclosed polynucleotides and proteins are also provided by the present invention. As herein, "species homologue" is a protein used a polynucleotide with a different species of origin from that of a given protein or polynucleotide, but with significant sequence similarity to the given protein or polynucleotide, as determined by those of skill in the art. Species homologs may be isolated and identified by making suitable probes or primers from the sequences provided herein and screening a suitable nucleic acid source from the desired species.

The invention also encompasses allelic variants of the disclosed polynucleotides or proteins; that is,

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naturally-occurring alternative forms of the isolated polynucleotide which also encode proteins which are identical, homologous, or related to that encoded by the polynucleotides.

The invention also includes polynucleotides with sequences complementary to those of the polynucleotides disclosed herein.

The present invention also includes polynucleotides capable of hybridizing under reduced stringency conditions, more preferably stringent conditions, and most preferably highly stringent conditions, polynucleotides described herein. Examples of stringency conditions are shown in the table below: highly stringent conditions are those that are at least as stringent as, for example, conditions A-F; stringent conditions are at least as stringent as, for example, conditions G-L; and reduced stringency conditions are at least as stringent as, for example, conditions M-R.

Table 32

| Stringency | Poly-      | Hybrid | Hybridization Temperature | Wash                    |
|------------|------------|--------|---------------------------|-------------------------|
| Condition  | nucleotide | Length | and Buffer <sup>†</sup>   | Temperature             |
| ·          | Hybrid     | (bp) * |                           | and Buffer'             |
| A          | DNA: DNA   | ≥50    | 65°C; 1×SSC -or-          | 65°C;                   |
|            |            |        | 42°C; 1×SSC,50%           | 0.3×SSC                 |
|            |            |        | formamide                 |                         |
| В          | DNA: DNA   | <50    | T <sub>B</sub> *; 1×SSC   | T <sub>B</sub> *; 1×SSC |
| С          | DNA: RNA   | ≥50    | 67°C; 1×SSC -or-          | 67°C;                   |
|            |            |        | 45°C; 1×SSC,50%           | 0.3×SSC                 |
|            |            |        | formamide                 |                         |
| D          | DNA: RNA   | <50    | T <sub>D</sub> *; 1×SSC   | T <sub>D</sub> *; 1×SSC |
| E          | RNA: RNA   | ≥50    | 70°C; 1×SSC -or-          | 70°C;                   |
|            |            |        | 50°C; 1×SSC,50%           | 0.3×SSC                 |
|            |            |        | formamide                 |                         |
| F          | RNA: RNA   | <50    | T <sub>F</sub> *; 1×SSC   | T <sub>F</sub> *; 1×SSC |
| G          | DNA: DNA   | ≥50    | 65°C; 4×SSC -or-          | 65°C; 1×SSC             |
|            |            |        | 42°C; 4×SSC,50%           |                         |
|            |            |        | formamide                 |                         |
| H          | DNA: DNA   | <50    | T <sub>H</sub> *; 4×SSC   | T <sub>H</sub> *; 4×SSC |
| I          | DNA: RNA   | ≥50    | 67°C; 4×SSC -or-          | 67°C; 1×SSC             |
|            |            |        | 45°C; 4×SSC,50%           |                         |
|            |            |        | formamide                 |                         |
| J          | DNA: RNA   | <50    | T <sub>J</sub> *; 4×SSC   | T <sub>J</sub> *; 4×SSC |
| K          | RNA: RNA   | ≥50    | 70°C; 4×SSC -or-          | 67°C; 1×SSC             |
|            |            |        | 50°C; 4×SSC,50%           |                         |
|            |            |        | formamide                 |                         |
| L          | RNA: RNA   | <50    | T <sub>L</sub> *; 2×SSC   | T <sub>t</sub> *; 2×SSC |
| М          | DNA: DNA   | ≥50    | 50°C; 4×SSC -or-          | 50°C; 2×SSC             |
|            |            |        | 40°C; 6×SSC,50%           |                         |
|            |            |        | formamide                 |                         |
| N          | DNA: DNA   | <50    | T <sub>N</sub> *; 6×SSC   | T <sub>N</sub> *; 6×SSC |
| 0          | DNA: RNA   | ≥50    | 55°C; 4×SSC -or-          | 55°C; 2×SSC             |
| 1          |            |        | 42°C; 6×SSC,50%           |                         |
|            |            |        | formamide                 |                         |
| P          | DNA: RNA   | <50    | T <sub>p</sub> *; 6×SSC   | T <sub>p</sub> *; 6×SSC |
| Q          | RNA: RNA   | ≥50    | 60°C; 4×SSC -or-          | 60°C; 2×SSC             |
|            |            |        | 45°C; 6×SSC,50%           |                         |
| <u> </u>   |            |        | formamide                 |                         |
| R          | RNA: RNA   | <50    | T <sub>R</sub> *; 4×SSC   | T <sub>R</sub> *; 4×SSC |

- † : The hybrid length is that anticipated for the hybridized region(s) of the hybridizing polynucleotides.

  When hybridizing a polynucleotide to a target polynucleotide of unknown sequence, the hybrid length is assumed to be that of the hybridizing polynucleotide. When polynucleotides of known sequence are hybridized, the hybrid length can be determined by aligning the sequences of the polynucleotides and identifying the region or regions of optimal sequence complementarity.
- t: SSPE (1×SSPE is 0.15M NaCl, 10mM NaH<sub>2</sub>PO<sub>4</sub>, and 1.25mM EDTA, pH7.4) can be substituted for SSC (1×SSC is 0.15M NaCl and 15mM sodium citrate) in the hybridization and wash buffers; washes are performed for 15 minutes after hybridization is complete.
- \*T<sub>B</sub> T<sub>R</sub>: The hybridization temperature for hybrids anticipated to be less than 50 base pairs in length should be 5-10°C less than the melting temperature (T<sub>m</sub>) of the hybrid, where T<sub>m</sub> is determined according to the following equations. For hybrids less than 18 base pairs in length,

  T<sub>m</sub>(°C)=2(#of A + T bases) + 4(# of G + C bases). For hybrids between 18 and 49 base pairs in length, T<sub>m</sub>(°C)=81.5 + 16.6(log<sub>10</sub>[Na<sup>+</sup>]) + 0.41 (%G+C) (600/N), where N is the number of bases in the hybrid, and [Na<sup>+</sup>] is the concentration of sodium ions in the hybridization buffer ([Na<sup>+</sup>] for 1×SSC=0.165M).

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Additional examples of stringency conditions for polynucleotide hybridization are provided in Sambrook, J., E.F. Fritsch, and T. Maniatis, 1989, Molecular Cloning: A Laboratory Manual, Cold Spring Harbor Laboratory Press, Cold Spring Harbor, NY, chapters 9 and 11, and Current Protocols in Molecular Biology, 1995, F.M. Ausubel et al., eds., John Wiley & Sons, Inc., sections 2.10 and 6.3-6.4, incorporated herein by reference.

Preferably, each such hybridizing polynucleotide has a length that is at least 25% (more preferably at least 50%, and most preferably at least 75%) of the length of the polynucleotide of the present invention to which it hybridizes, and has at least 60% sequence identity (more preferably, at least 75% identity; most preferably at least 90% or 95% identity) with the polynucleotide of the present invention to which it hybridizes, where sequence identity is determined by comparing the sequences of the hybridizing polynucleotides when aligned so as to maximize overlap and identity while minimizing sequence gaps.

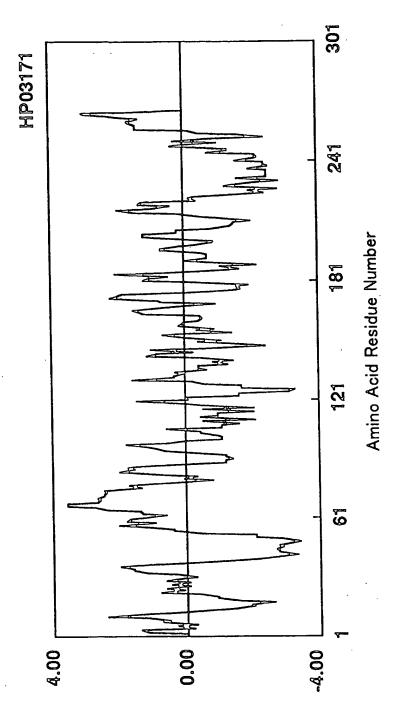
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## CLAIMS

- 1. A protein comprising any one of an amino acid sequence selected from the group consisting of SEQ ID NOS: 1 to 10, 31 to 40, 61 to 70, 91 to 100 and 121 to 130.
- 2. An isolated DNA encoding the protein according to Claim 1.
- 3. An isolated cDNA comprising any one of a base sequence selected from the group consisting of SEQ ID NOS: 11 to 20, 41 to 50, 71 to 80, 101 to 110 and 131 to 140.
  - 4. The cDNA according to Claim 3 consisting of any one of a base sequence selected from the group consisting of SEQ ID NOS: 21 to 30, 51 to 60, 81 to 90, 111 to 120 and 141 to 150.
- 5. An expression vector that is capable of expressing the DNA according to any one of Claim 2 to Claim 4 by in vitro translation or in eukaryotic cells.
  - 6. A transformed eukaryotic cell that is capable of expressing the DNA according to any one of Claim 2 to Claim 4 and of producing the protein according to Claim 1.
    - 7. An antibody directed to the protein according to Claim 1.

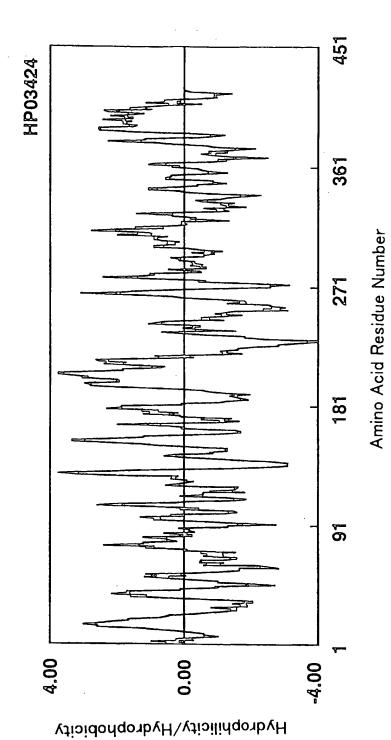




Hydrophilicity/Hydrophobicity

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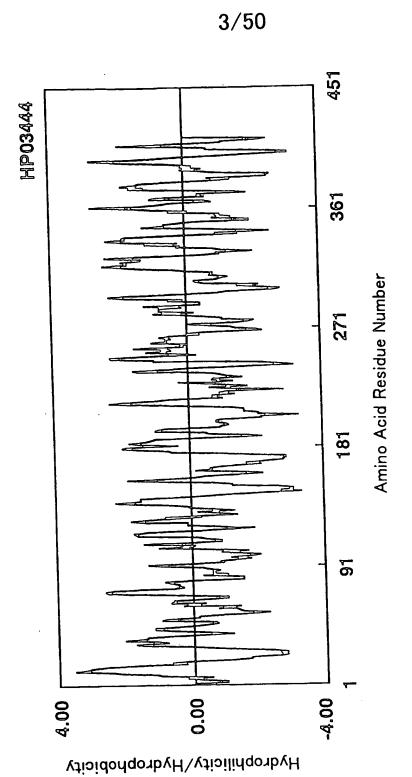


Fig.3

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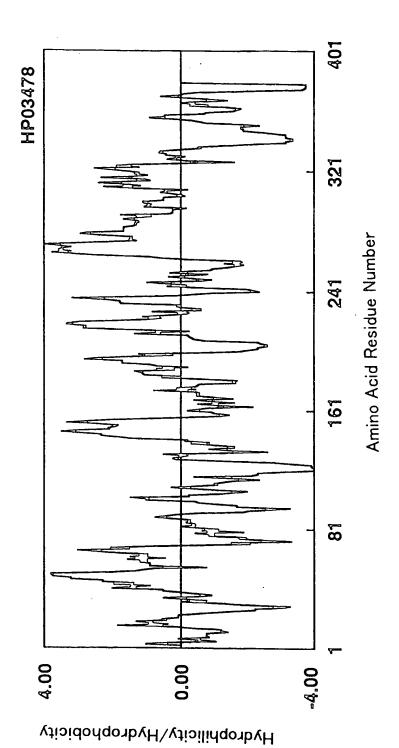


Fig.4

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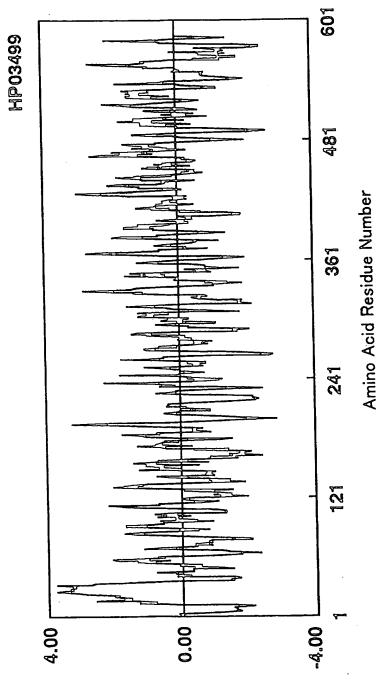


Fig.5

Hydrophilicity/Hydrophobicity

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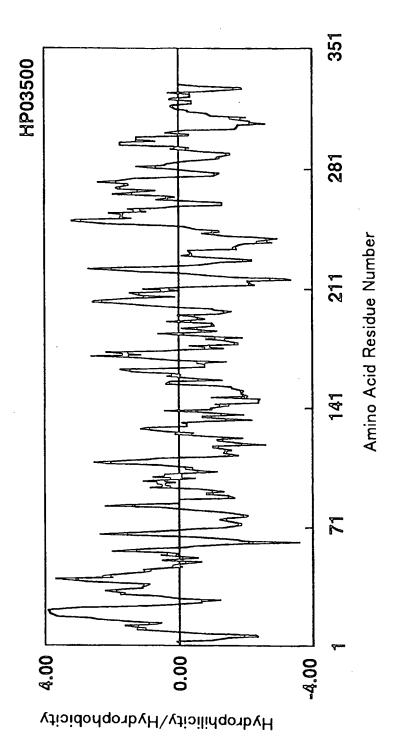
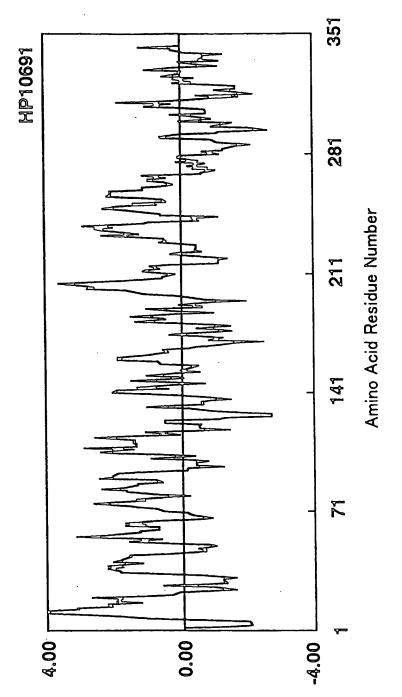


Fig.6



Hydrophilicity/Hydrophobicity

Fig.7



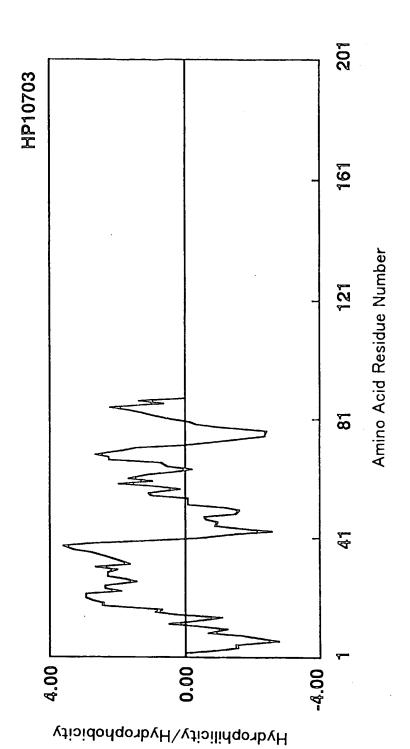
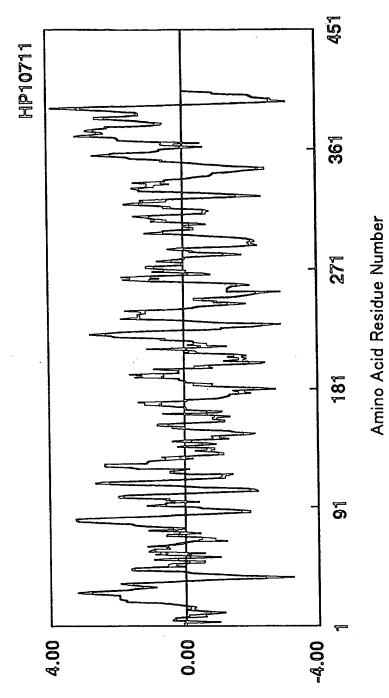


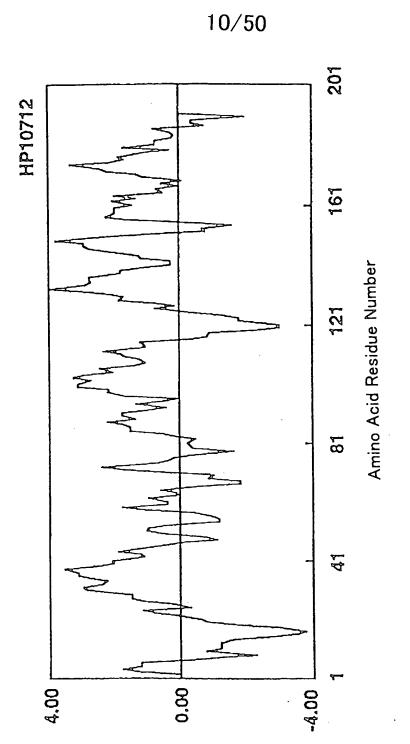
Fig.8

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Hydrophilicity/Hydrophobicity

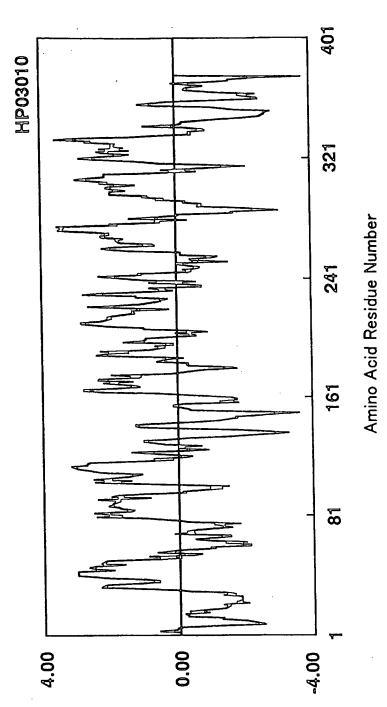
Fig.9



Hydrophilicity/Hydrophobicity

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Hydrophilicity/Hydrophobicity

Fig. 1



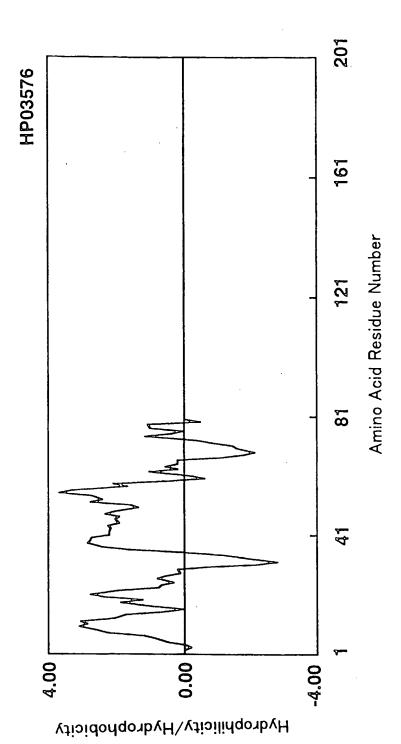


Fig. 1



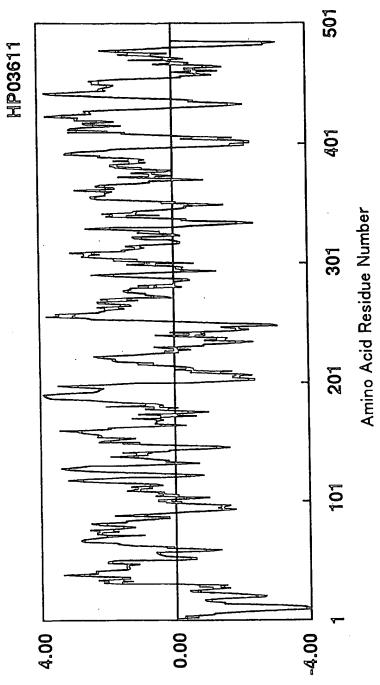


Fig.13

Hydrophilicity/Hydrophobicity



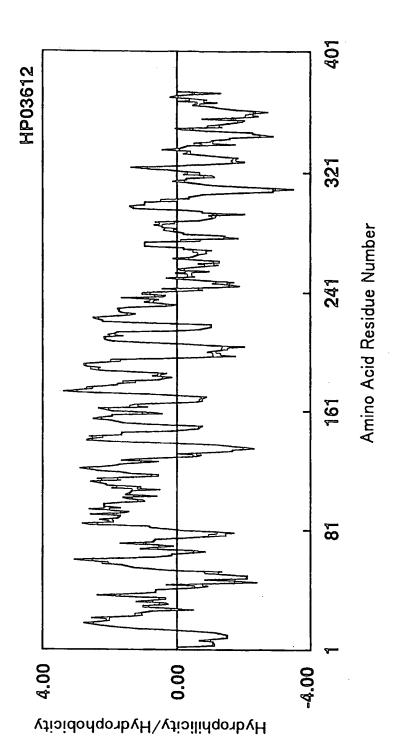


Fig. 14

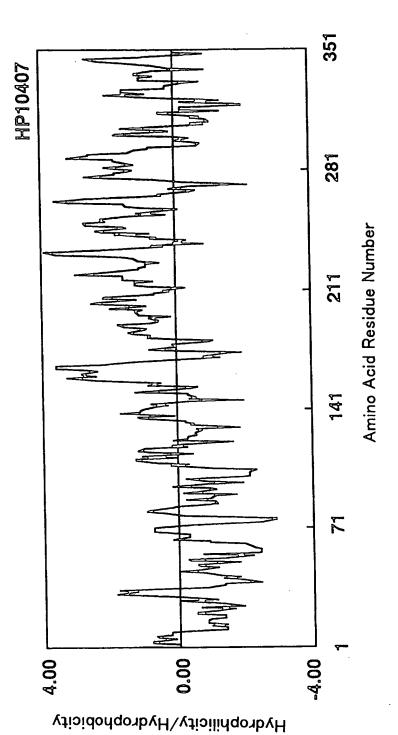


Fig.15

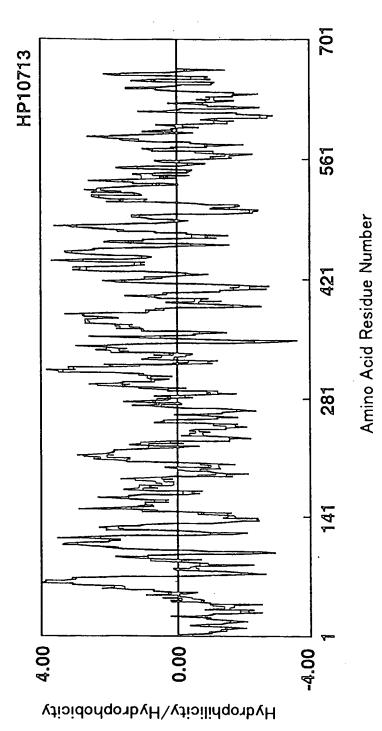
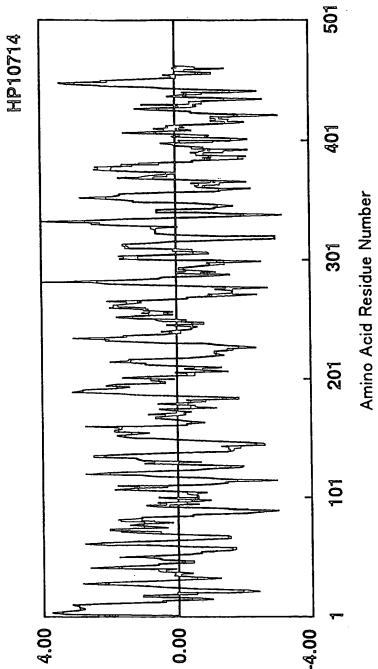


Fig.16

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Hydrophilicity/Hydrophobicity

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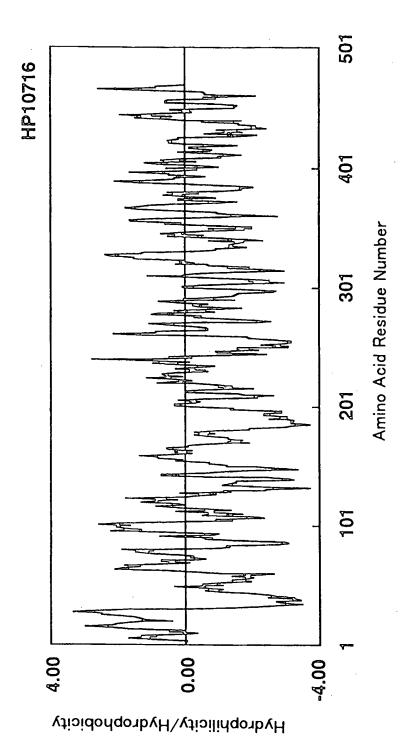


Fig. 18

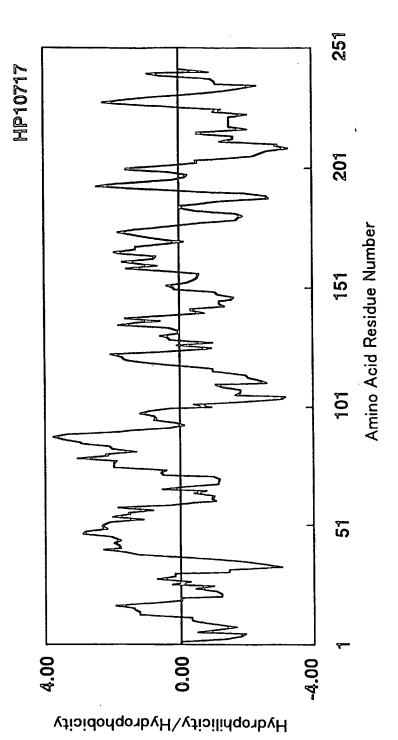
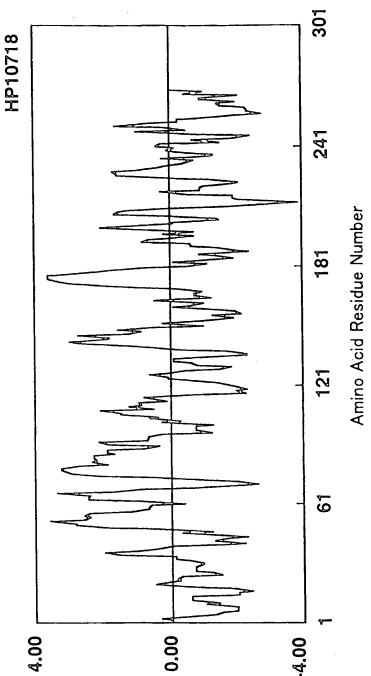


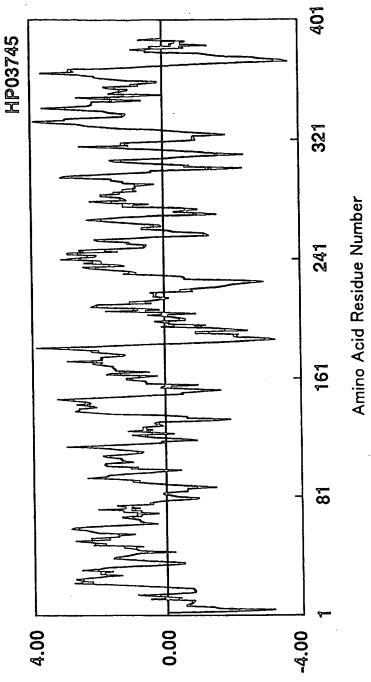
Fig. 19





Hydrophilicity/Hydrophobicity





Hydrophilicity/Hydrophobicity

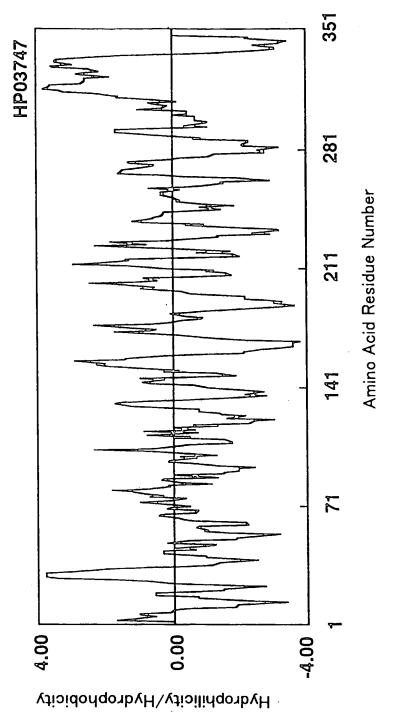


Fig.22



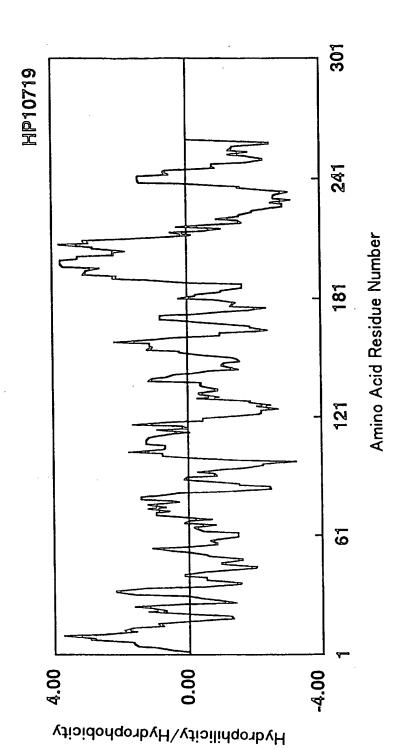


Fig.23

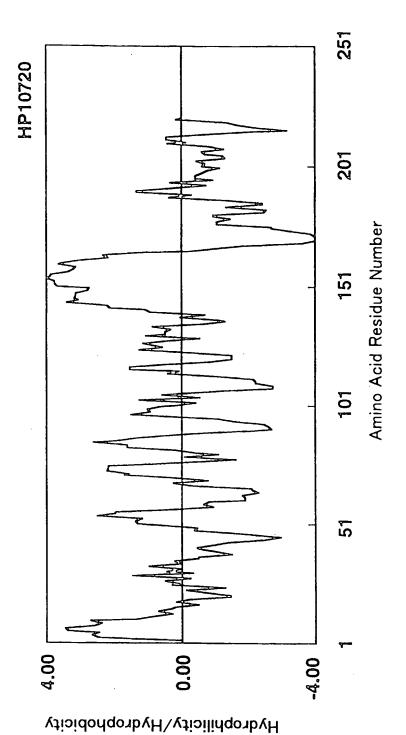


Fig.24

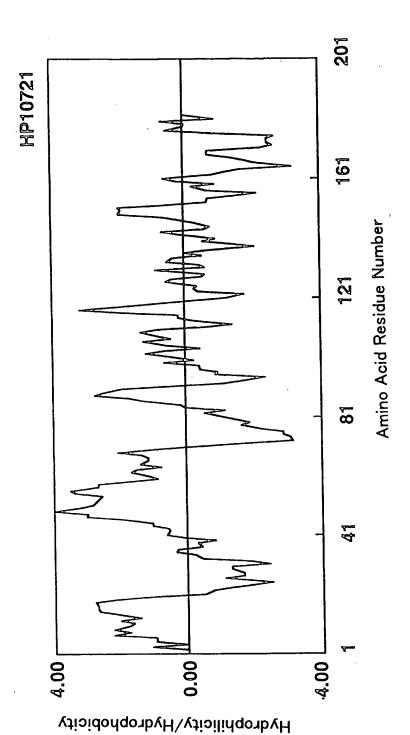


Fig.25

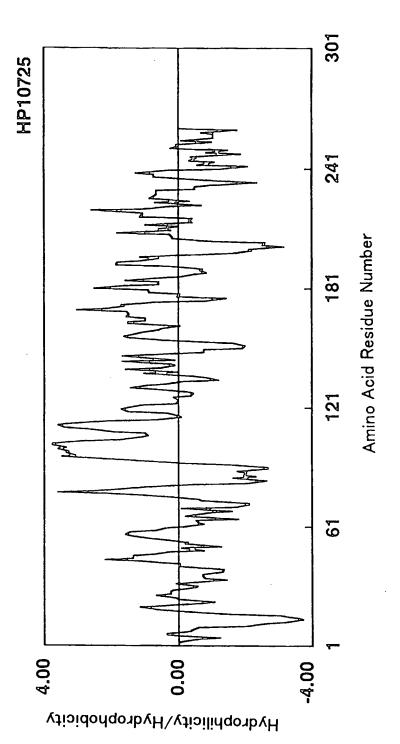
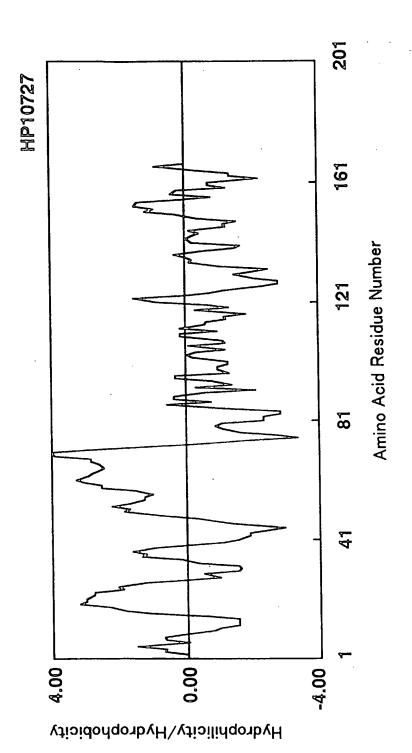


Fig.26





-ig.27

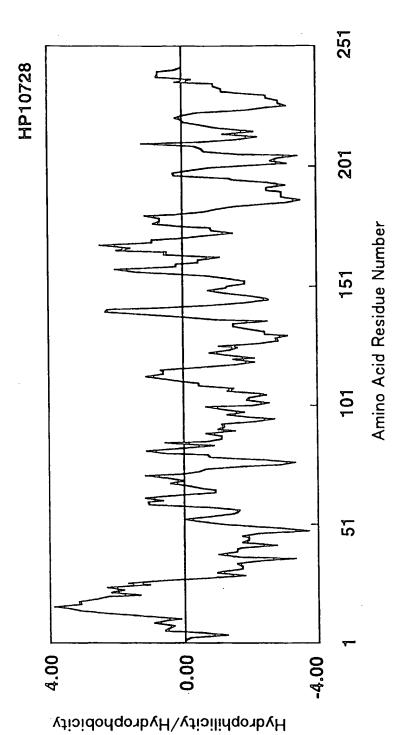
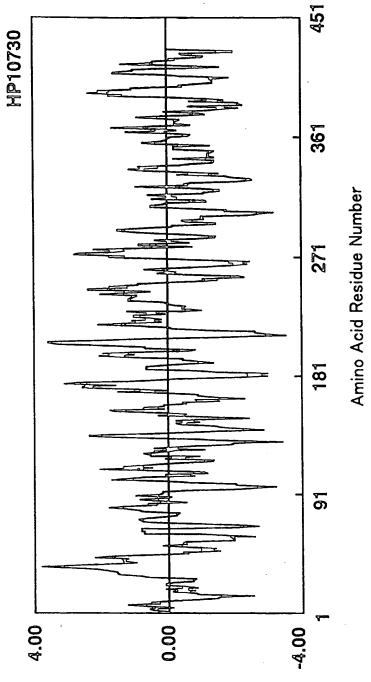


Fig.28



Hydrophilicity/Hydrophobicity

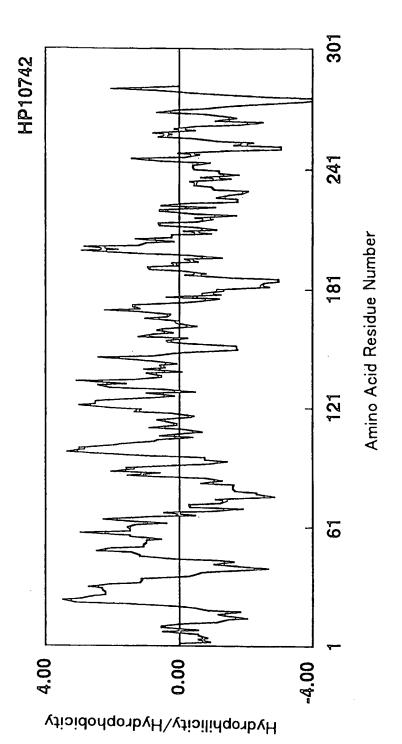
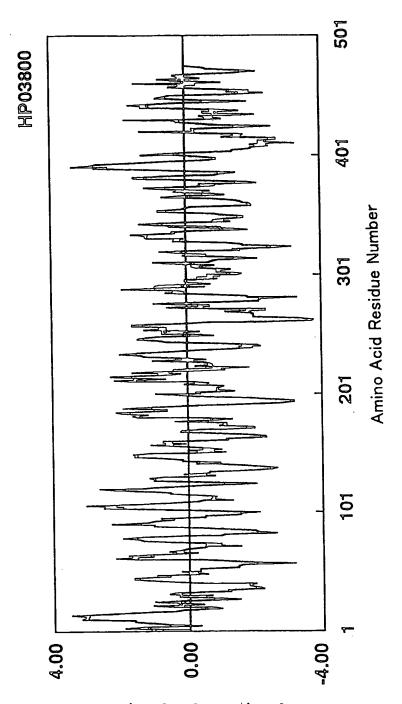


Fig. 30

WO 01/12660 PCT/JP00/05356





Hydrophilicity/Hydrophobicity



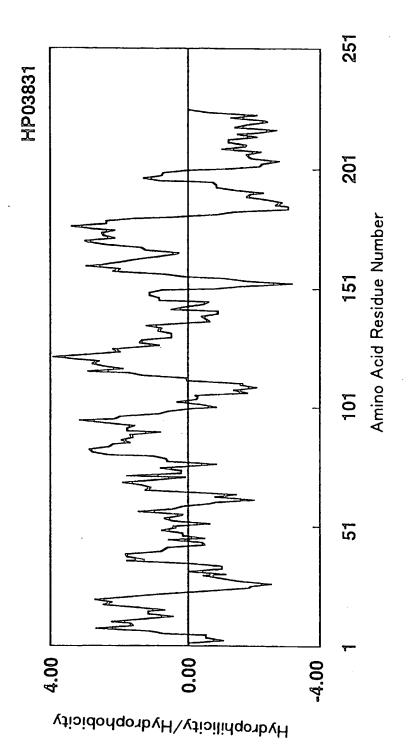
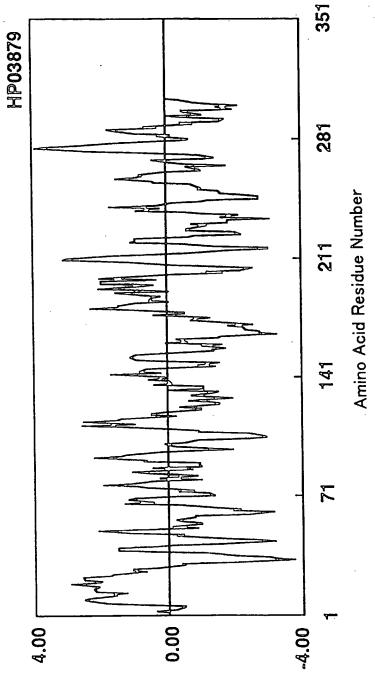


Fig.32



Hydrophilicity/Hydrophobicity

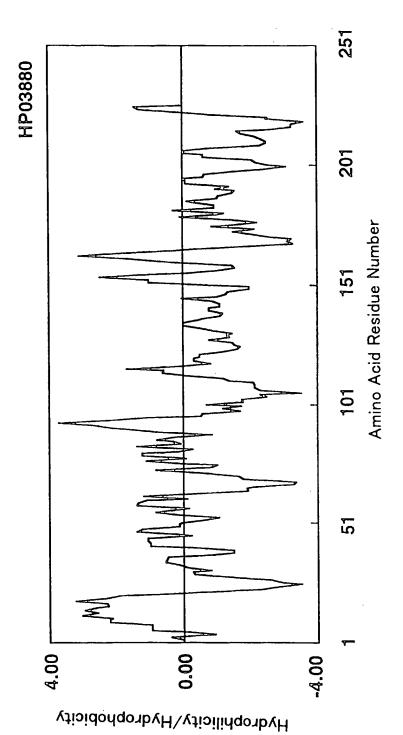


Fig.34

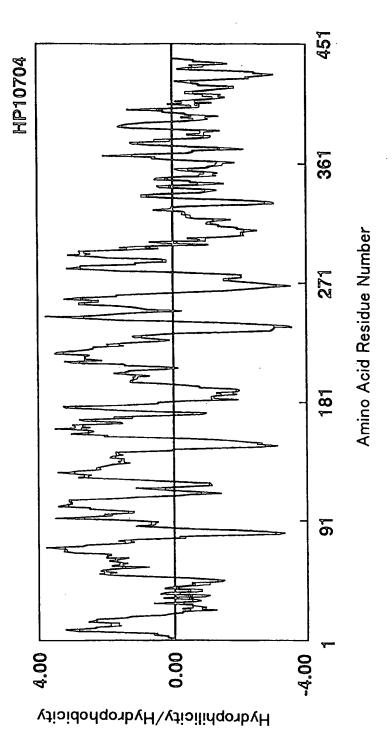


Fig.35

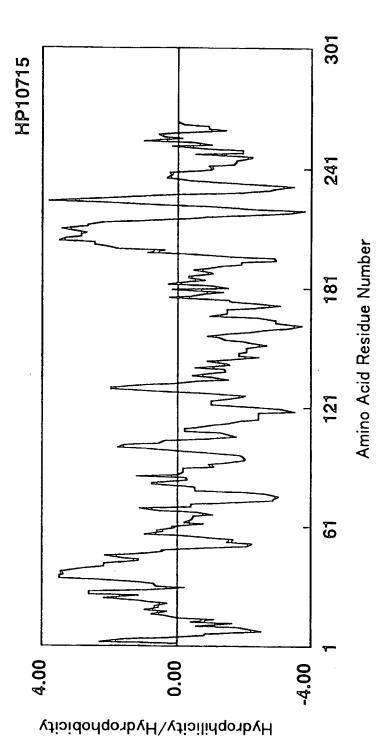


Fig.36

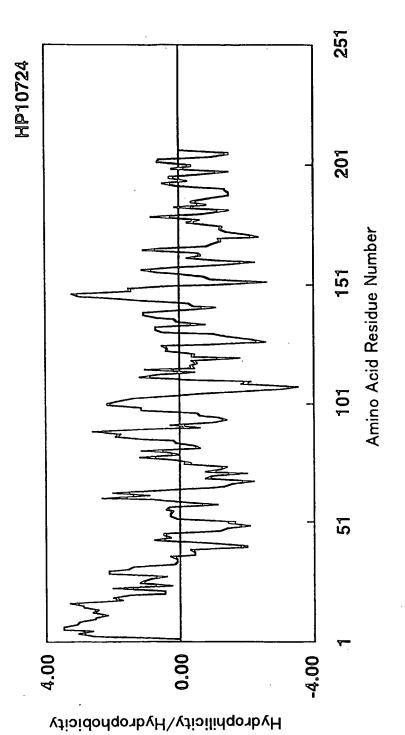


Fig.37

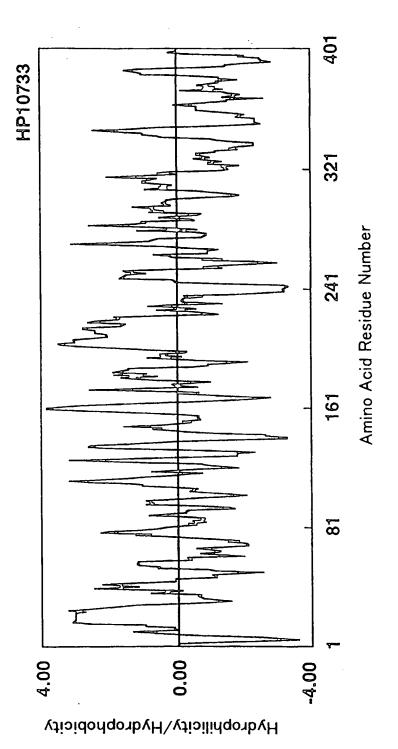


Fig.38

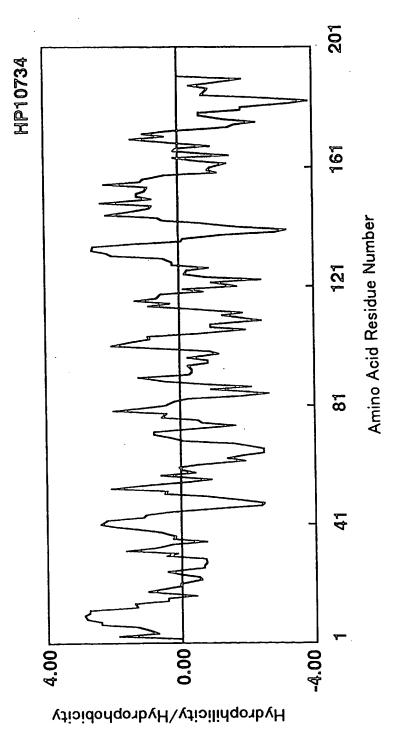


Fig.39

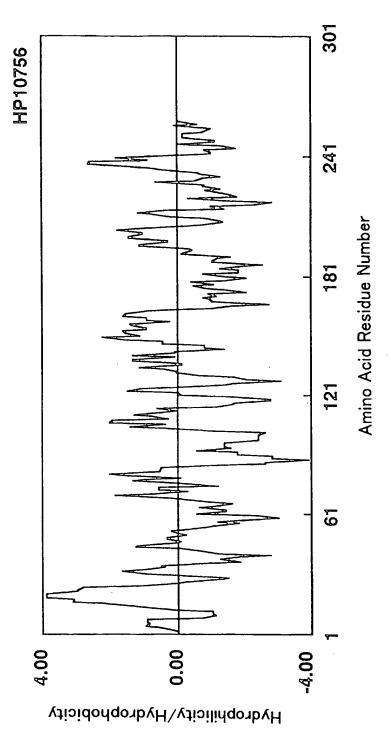


Fig.40

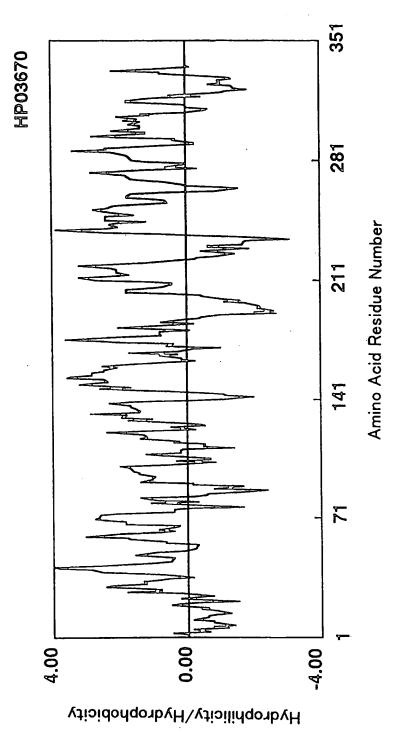
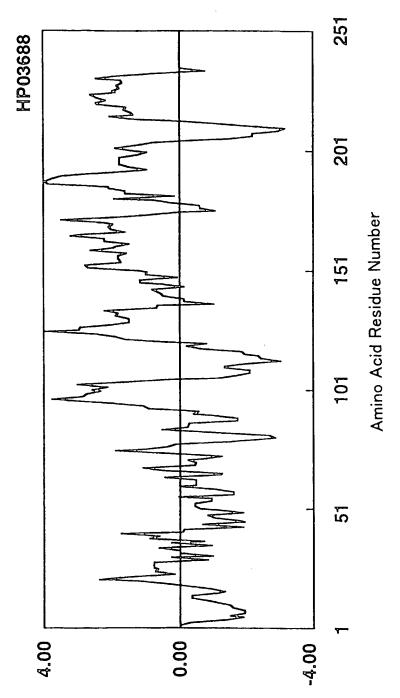


Fig.4





Hydrophilicity/Hydrophobicity

Fig.42

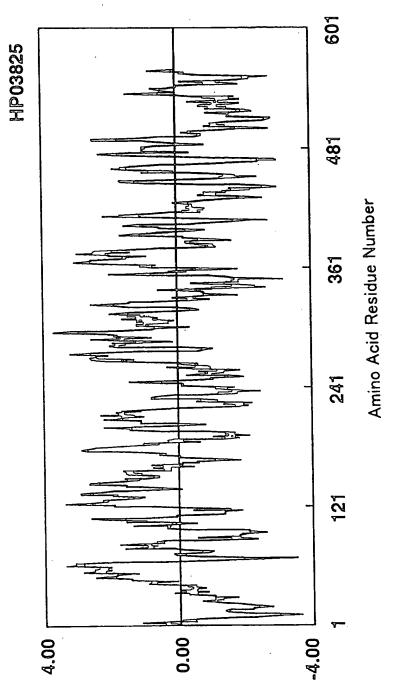


Fig.4

Hydrophilicity/Hydrophobicity

44/50

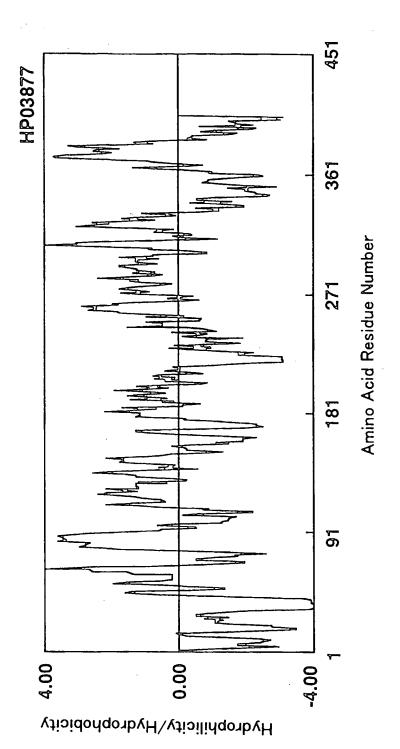


Fig.44

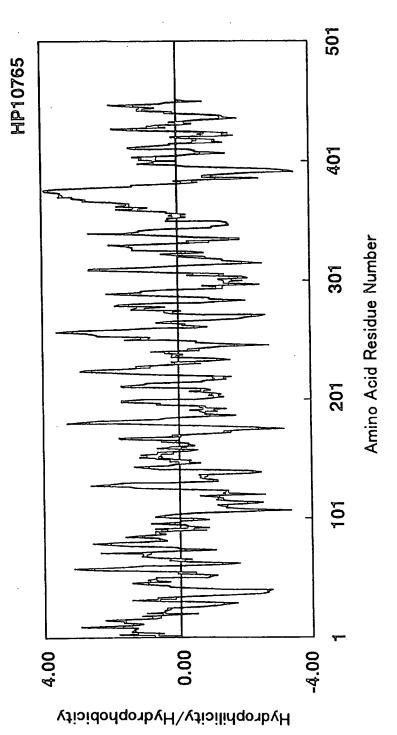


Fig.45



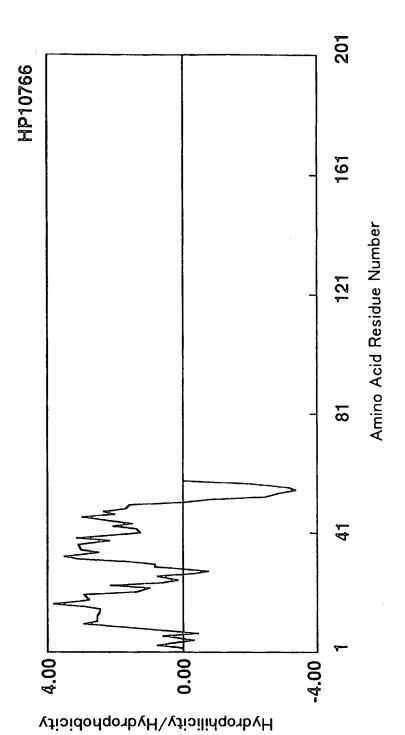
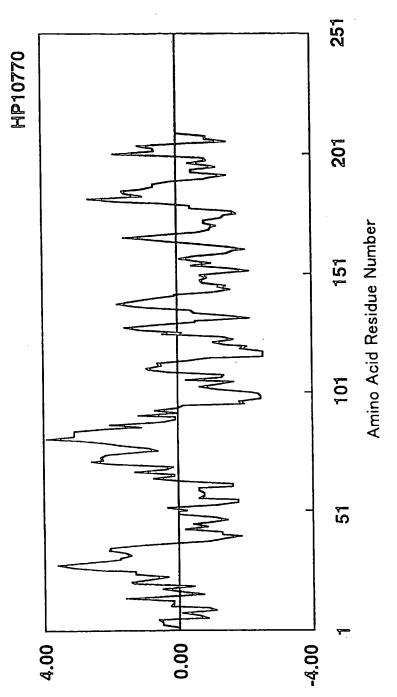


Fig.46



Hydrophilicity/Hydrophobicity

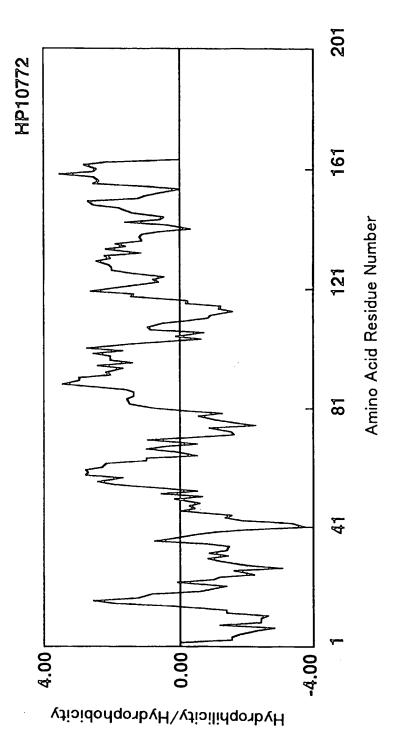


Fig.48

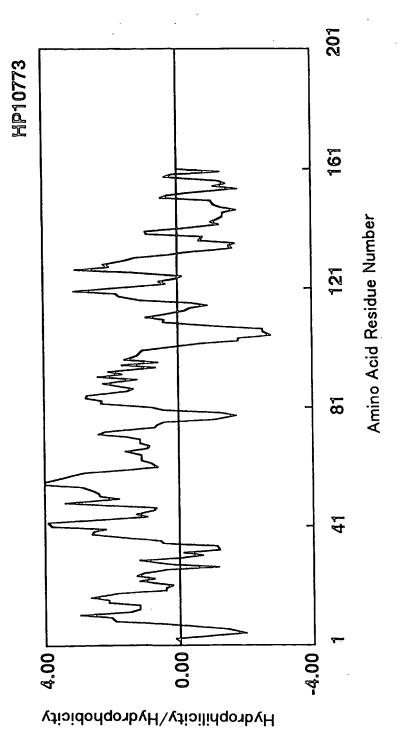
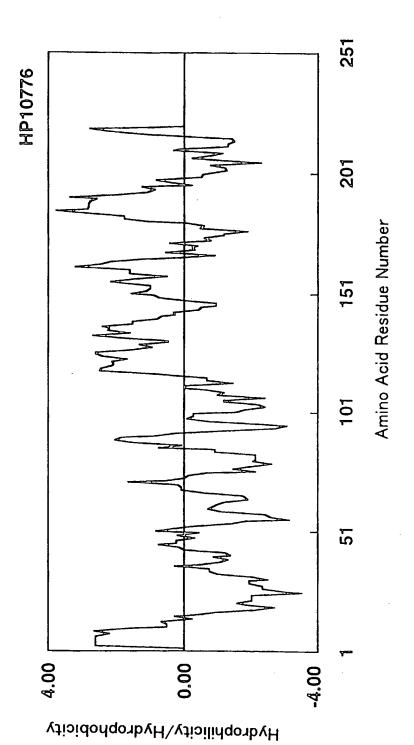


Fig.49



### SEQUENCE LISTING

<110> Sagami Chemical Research Center,
Protegene Inc.

<120> Human proteins having hydrophobic domains and DNAs encoding these proteins

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<150> JP 11-230344

<151> 1999−08−17

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<150> JP 11-281132

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Glu Ile Leu Leu Thr Pro Ala Arg Glu Glu Gln Pro Pro Gln His Arg

35 40 45

Ser Lys Arg Gly Ser Ser Val Gly Gly Val Cys Tyr Leu Ser Met Gly

50 55 60

Met Val Val Leu Leu Met Gly Leu Val Phe Ala Ser Val Tyr Ile Tyr

65 70 75 80

Arg Tyr Phe Phe Leu Ala Gln Leu Ala Arg Asp Asn Phe Phe Arg Cys

90 95

Gly Val Leu Tyr Glu Asp Ser Leu Ser Ser Gln Val Arg Thr Gln Met

100 105 110

Glu Leu Glu Glu Asp Val Lys Ile Tyr Leu Asp Glu Asn Tyr Glu Arg

115 120 125

Ile Asn Val Pro Val Pro Gln Phe Gly Gly Gly Asp Pro Ala Asp Ile

130 135 / 140

Ile His Asp Phe Gln Arg Gly Leu Thr Ala Tyr His Asp Ile Ser Leu Asp Lys Cys Tyr Val Ile Glu Leu Asn Thr Thr Ile Val Leu Pro Pro Arg Asn Phe Trp Glu Leu Leu Met Asn Val Lys Arg Gly Thr Tyr Leu Pro Gln Thr Tyr Ile Ile Gln Glu Glu Met Val Val Thr Glu His Val Ser Asp Lys Glu Ala Leu Gly Ser Phe Ile Tyr His Leu Cys Asn Gly Lys Asp Thr Tyr Arg Leu Arg Arg Arg Ala Thr Arg Arg Arg Ile Asn Lys Arg Gly Ala Lys Asn Cys Asn Ala Ile Arg His Phe Glu Asn Thr Phe Val Val Glu Thr Leu Ile Cys Gly Val Val <210> 2 <211> 419 <212> PRT <213> Homo sapiens <400> 2 Met Ser Cys Ala Gly Arg Ala Gly Pro Ala Arg Leu Ala Ala Leu Ala Leu Leu Thr Cys Ser Leu Trp Pro Ala Arg Ala Asp Asn Ala Ser Gln

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|-----|-----|-----|-----|-----|-----|------------|-----|-----|------|------------|-----|-----|-----|-----|-----|
| Glu | Tyr | Tyr | Thr | Ala | Leu | Ile        | Asn | Val | Thr  | Val        | Gln | Glu | Prọ | Gly | Arg |
|     |     | 35  |     |     |     |            | 40  | •   |      |            |     | 45  |     |     |     |
| Gly | Ala | Pro | Leu | Thr | Phe | Arg        | Ile | Asp | Arg  | Gly        | Arg | Tyr | Gly | Leu | Asp |
|     | 50  |     |     |     |     | <b>5</b> 5 |     |     |      |            | 60  |     |     |     |     |
| Ser | Pro | Lys | Ala | Glu | Val | Arg        | Gly | Gln | Val  | Leu        | Ala | Pro | Leu | Pro | Leu |
| 65  |     |     |     |     | 70  |            |     |     |      | <b>7</b> 5 |     |     |     |     | 80  |
| His | Gly | Val | Ala | Asp | His | Leu        | Gly | Cys | Asp  | Pro        | Gln | Thr | Arg | Phe | Phe |
|     |     |     |     | 85  |     |            |     |     | 90   |            |     |     |     | 95  |     |
| Val | Pro | Pro | Asn | Ile | Lys | Gln        | Trp | Ile | Ala  | Leu        | Leu | Gln | Arg | Gly | Asn |
|     |     |     | 100 |     |     |            |     | 105 |      |            |     |     | 110 |     |     |
| Cys | Thr | Phe | Lys | Glu | Lys | Ile        | Ser | Arg | Ala  | Ala        | Phe | His | Asn | Ala | Val |
|     |     | 115 |     |     |     |            | 120 |     |      |            |     | 125 |     |     |     |
| Ala | Val | Val | Ile | Tyr | Asn | Asn        | Lys | Ser | Lys  | Glu        | Glu | Pro | Val | Thr | Met |
|     | 130 |     |     |     | •   | 135        |     |     |      |            | 140 |     |     |     |     |
| Thr | His | Pro | Gly | Thr | Gly | Asp        | Ile | Ile | Ala  | Val        | Met | Ile | Thr | Glu | Leu |
| 145 |     |     |     |     | 150 |            |     |     |      | 155        |     |     |     |     | 160 |
| Arg | Gly | Lys | Asp | Ile | Leu | Ser        | Tyr | Leu | Glu  | Lys        | Asn | Ile | Ser | Val | Gln |
|     |     |     |     | 165 |     |            |     |     | 170  |            |     |     |     | 175 |     |
| Met | Thr | Ile | Ala | Val | Gly | Thr        | Arg | Met | Pro  | Pro        | Lys | Asn | Phe | Ser | Arg |
|     |     |     | 180 |     |     |            |     | 185 |      |            |     |     | 190 |     |     |
| Gly | Ser | Leu | Val | Phe | Val | Ser        | Ile | Ser | Phe  | Ile        | Val | Leu | Met | Ile | Ile |
|     |     | 195 |     |     |     |            | 200 |     |      |            |     | 205 |     |     |     |
| Ser | Ser | Ala | Trp | Leu | Ile | Phe        | Tyr | Phe | Ile  | Gln        | Lys | Ile | Arg | Tyr | Thr |
|     | 210 |     |     |     |     | 215        |     | /   | ننمو |            | 220 |     |     |     |     |

| Asn | Ala | Arg | Asp   | Arg   | Asn | Gln   | Arg | Arg | Leu | Gly | Asp | Ala | Ala | Lys   | Lys   |
|-----|-----|-----|-------|-------|-----|-------|-----|-----|-----|-----|-----|-----|-----|-------|-------|
| 225 |     |     |       |       | 230 |       |     |     |     | 235 |     |     |     |       | 240   |
| Ala | Ile | Ser | Lys   | Leu   | Thr | Thr   | Arg | Thr | Val | Lys | Lys | Gly | Asp | Lys   | Glu   |
|     |     |     |       | 245   |     |       |     |     | 250 |     |     |     |     | 255   |       |
| Thr | Asp | Pro | Asp   | Phe   | Asp | His   | Cys | Ala | Val | Cys | Ile | Glu | Ser | Tyr   | Lys   |
|     |     |     | 260   |       |     |       |     | 265 |     |     |     |     | 270 |       |       |
| Gln | Asn | Asp | Val   | Val   | Arg | Ile   | Leu | Pro | Cys | Lys | His | Val | Phe | His   | Lys   |
|     |     | 275 |       |       |     |       | 280 |     |     |     |     | 285 |     |       |       |
| Ser | Cys | Val | Asp   | Pro   | Trp | Leu   | Ser | Glu | His | Cys | Thr | Cys | Pro | Met   | Cys   |
|     | 290 |     |       |       |     | 295   |     |     |     |     | 300 |     |     |       |       |
| Lys | Leu | Asn | Ile   | Leu   | Lys | Ala   | Leu | Gly | Ile | Val | Pro | Asn | Leu | Pro   | Cys   |
| 305 |     |     |       |       | 310 |       |     |     |     | 315 |     |     |     |       | 320   |
| Thr | Asp | Asn | Val   | Ala   | Phe | Asp   | Met | Glu | Arg | Leu | Thr | Arg | Thr | Gln   | Ala   |
|     |     |     |       | 325   |     |       |     |     | 330 |     |     |     |     | 335   |       |
| Val | Asn | Arg | Arg   | Ser   | Ala | Leu   | Gly | Asp | Leu | Ala | Gly | Asp | Asn | Ser   | Leu   |
|     |     |     | 340   |       |     |       |     | 345 |     |     |     |     | 350 |       |       |
| Gly | Leu | G1u | Pro   | Leu   | Arg | Thr   | Ser | Gly | Ile | Ser | Pro | Leu | Pro | Gln   | Asp   |
|     |     | 355 |       |       |     |       | 360 |     |     |     |     | 365 |     |       |       |
| Gly | Glu | Leu | Thr   | Pro   | Arg | Thr   | Gly | Glu | Ile | Asn | Ile | Ala | Val | Thr   | Lys   |
|     | 370 | )   |       |       | •   | 375   |     |     |     |     | 380 |     |     |       |       |
| Glu | Trp | Phe | : Ile | · Ile | Ala | Ser   | Phe | Gly | Leu | Leu | Ser | Ala | Leu | Thr   | Leu   |
| 385 | 5   |     |       |       | 390 | )     |     |     |     | 395 |     |     |     |       | 400   |
| Cys | Tyr | Met | : 11  | e Ile | Arg | , Ala | Thr | Ala | Ser | Leu | Asn | Ala | Asr | ı Glu | ı Val |
|     |     |     |       | 405   | 5   |       |     |     | 410 | )   |     |     |     | 415   | 5     |
|     |     |     |       |       |     |       |     | _   |     |     |     |     |     |       |       |

Glu Trp Phe

| <210 | )> 3  |       |       |     |     |     | -   |     |     |     |     |     |     |     |      |
|------|-------|-------|-------|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|------|
| <211 | > 41  | 5     |       |     |     |     |     |     |     |     |     |     |     |     |      |
| <212 | 2> PF | T     |       |     |     |     |     |     |     |     |     |     |     |     |      |
| <213 | 3> Ho | omo s | sapie | ens |     |     |     |     |     |     |     |     |     |     |      |
| <400 | )> 3  |       |       |     |     |     |     |     |     |     | -   |     |     |     |      |
| Met  | Arg   | Gly   | Ala   | Asn | Ala | Trp | Ala | Pro | Leu | Cys | Leu | Leu | Leu | Ala | Ala  |
| 1    |       |       |       | 5   |     |     |     |     | 10  |     |     |     |     | 15  |      |
| Ala  | Thr   | Gln   | Leu   | Ser | Arg | Gln | Gln | Ser | Pro | Glu | Arg | Pro | Val | Phe | Thr  |
|      |       |       | 20    |     |     |     |     | 25  |     |     |     |     | 30  |     |      |
| Cys  | Gly   | Gly   | Ile   | Leu | Thr | Gly | Glu | Ser | Gly | Phe | Ile | Gly | Ser | Glu | Gly  |
|      |       | 35    |       |     |     |     | 40  |     |     |     |     | 45  |     |     |      |
| Phe  | Pro   | Gly   | Val   | Tyr | Pro | Pro | Asn | Ser | Lys | Cys | Thr | Trp | Lys | Ile | Thr  |
|      | 50    |       |       |     |     | 55  |     |     |     |     | 60  |     |     |     |      |
| Val  | Pro   | Glu   | Gly   | Lys | Val | Val | Val | Leu | Asn | Phe | Arg | Phe | Ile | Asp | Leu  |
| 65   |       |       |       |     | 70  |     |     |     |     | 75  |     |     |     |     | 80   |
| Glu  | Ser   | Asp   | Asn   | Leu | Cys | Arg | Tyr | Asp | Phe | Val | Asp | Val | Tyr | Asn | Gly  |
|      |       |       |       | 85  |     |     |     |     | 90  |     |     |     |     | 95  |      |
| His  | Ala   | Asn   | Gly   | G1n | Arg | Ile | Gly | Arg | Phe | Cys | Gly | Thr | Phe | Arg | Pro. |
|      |       |       | 100   |     |     |     |     | 105 |     |     |     |     | 110 |     |      |
| Gly  | Ala   | Leu   | Val   | Ser | Ser | Gly | Asn | Lys | Met | Met | Val | Gln | Met | Ile | Ser  |
|      |       | 115   |       |     |     |     | 120 |     |     |     |     | 125 |     |     |      |
| Asp  | Ala   | Asn   | Thr   | Ala | Gly | Asn | Gly | Phe | Met | Ala | Met | Phe | Ser | Ala | Ala  |
|      | 130   |       |       |     |     | 135 |     |     |     |     | 140 |     |     |     |      |
| Glu  | Pro   | Asn   | Glu   | Arg | Gly | Asp | G1n | Tyr | Čys | Gly | Gly | Leu | Leu | Asp | Arg  |

| 145 |      |       |       |       | 150   |       |       |           |               | 155   |       |       |          |       | 160   |
|-----|------|-------|-------|-------|-------|-------|-------|-----------|---------------|-------|-------|-------|----------|-------|-------|
| Pro | Ser  | Gly   | Ser   | Phe   | Lys   | Thr   | Pro   | Asn       | Trp           | Pro   | Asp   | Arg   | Asp      | Tyr   | Pro   |
|     |      |       |       | 165   |       |       |       |           | 170           |       |       |       |          | 175   |       |
| Ala | Gly  | Val   | Thr   | Cys   | Val   | Trp   | His   | Ile       | Val           | Ala   | Pro   | Lys   | Asn      | Gln   | Leu   |
|     |      |       | 180   |       |       |       |       | 185       |               |       |       |       | 190      |       |       |
| Ile | Glu  | Leu   | Lys   | Phe   | Glu   | Lys   | Phe   | Asp       | Val           | Glu   | Arg   | Asp   | Asn      | Tyr   | Cys   |
|     |      | 195   |       |       |       |       | 200   |           |               |       |       | 205   |          | •     |       |
| Arg | Tyr  | Asp   | Tyr   | Val   | Ala   | Val   | Phe   | Asn       | Gly           | Gly   | Glu   | Val   | Asn      | Asp   | Ala   |
|     | 210  |       |       |       |       | 215   |       |           |               |       | 220   |       |          |       |       |
| Arg | Arg  | Ile   | Gly   | Lys   | Tyr   | Cys   | Gly   | Asp       | Ser           | Pro   | Pro   | Ala   | Pro      | Ile   | Val   |
| 225 |      |       |       |       | 230   |       |       |           |               | 235   |       |       |          |       | 240   |
| Ser | Glu  | Arg   | : Asn | Glu   | Leu   | Leu   | Ile   | Gln       | Phe           | Leu   | Ser   | Asp   | Leu      | Ser   | Leu   |
|     |      |       |       | 245   | ;     |       |       |           | 250           |       |       |       |          | 255   |       |
| Thr | Ala  | Asp   | Gly   | Phe   | · Ile | Gly   | His   | Tyr       | Ile           | Phe   | Arg   | Pro   | Lys      | Lys   | Leu   |
|     |      |       | 260   | )     |       |       |       | 265       |               |       |       |       | 270      |       |       |
| Pro | Thr  | Thi   | Thi   | - Glu | ı Gln | Pro   | Val   | Thr       | Thr           | Thr   | Phe   | Pro   | Val      | Thr   | Thr   |
|     |      | 275   | 5     |       |       |       | 280   | )         |               |       |       | 285   | <u>,</u> |       |       |
| Gly | Leu  | ı Lys | s Thi | r Thr | . Val | Ala   | Leu   | ı Cys     | Gln           | Gln   | Lys   | Cys   | Arg      | Arg   | Thr   |
|     | 290  | )     |       |       |       | 298   | 5     |           |               |       | 300   | ) .   |          |       |       |
| Gly | Thi  | : Le  | u Gli | u Gly | y Asr | ı Tyı | r Cys | s Ser     | : Ser         | - Asp | Phe   | va]   | l Leu    | Ala   | Gly   |
| 305 | ;    |       |       |       | 310   | )     |       |           |               | 315   | 5     |       |          |       | 320   |
| Thr | · Va | l II  | e Th  | r Thi | r Ile | e Thi | r Arį | g Ası     | p Gly         | y Sei | : Lei | ı His | s Ala    | Thi   | . Val |
|     |      |       |       | 32    |       |       |       |           | 330           |       |       |       |          | 339   |       |
| Sei | - Il | e Il  | e As  | n Il  | e Ty: | r Ly  | s Gl  | u G1;     | y <u>A</u> sı | n Lei | ı Ala | a Il  | e Gli    | ı Glı | n Ala |
|     |      |       | 34    |       |       |       |       | <b>34</b> | -             |       |       |       | 350      |       |       |

| Gly  | Lys       | Asn   | Met   | Ser | Ala | Arg       | Leu | Thr | Val | Val | Cys       | Lys | Gln | Cys | Pro |
|------|-----------|-------|-------|-----|-----|-----------|-----|-----|-----|-----|-----------|-----|-----|-----|-----|
|      |           | 355   |       |     |     |           | 360 |     |     |     |           | 365 |     |     |     |
| Leu  | Leu       | Arg   | Arg   | Gly | Leu | Asn       | Tyr | Ile | Ile | Met | Gly       | Gln | Val | Gly | Glu |
|      | 370       |       |       |     |     | 375       |     |     |     |     | 380       |     |     |     |     |
| Asp  | Gly       | Arg   | Gly   | Lys | Ile | Met       | Pro | Asn | Ser | Phe | Ile       | Met | Met | Phe | Lys |
| 385  |           |       |       |     | 390 |           |     |     |     | 395 |           |     |     |     | 400 |
| Thr  | Lys       | Asn   | Gln   | Lys | Leu | Leu       | Asp | Ala | Leu | Lys | Asn       | Lys | Gln | Cys |     |
|      |           |       |       | 405 |     |           |     |     | 410 |     |           |     |     | 415 |     |
|      |           |       |       |     |     |           |     |     |     |     |           |     |     |     |     |
| <210 | )> 4      |       |       |     |     |           |     |     |     |     |           |     |     |     |     |
| <21  | 1> 38     | 30    |       |     |     |           |     |     |     |     |           |     |     |     |     |
| <212 | 2> PF     | T7    |       |     |     |           |     |     |     |     |           |     |     | ٠   |     |
| <213 | 3> Ho     | omo s | sapie | ens |     |           |     |     |     |     |           |     |     |     |     |
| <400 | )> 4      |       |       |     |     |           |     |     |     |     |           |     |     |     |     |
| Met  | Leu       | Gln   | Thr   | Leu | Tyr | Asp       | Tyr | Phe | Trp | Trp | Glu       | Arg | Leu | Trp | Leu |
| 1    |           |       |       | 5   |     |           |     |     | 10  |     |           |     |     | 15  |     |
| Pro  | Val       | Asn   | Leu   | Thr | Trp | Ala       | Asp | Leu | Glu | Asp | Arg       | Asp | Gly | Arg | Va1 |
|      |           |       | 20    |     |     |           |     | 25  |     |     |           |     | 30  |     |     |
| Tyr  | Ala       | Lys   | Ala   | Ser | Asp | Leu       | Tyr | Ile | Thr | Leu | Pro       | Leu | Ala | Leu | Leu |
|      |           | 35    |       |     |     |           | 40  |     |     |     |           | 45  |     |     |     |
| Phe  |           |       |       |     |     |           |     |     |     |     |           |     |     |     |     |
|      | Leu       | Ile   | Val   | Arg | Tyr | Phe       | Phe | Glu | Leu | Tyr | Val       | Ala | Thr | Pro | Leu |
|      | Leu<br>50 | Ile   | Val   | Arg | Tyr | Phe<br>55 | Phe | Glu | Leu | Tyr | Val<br>60 | Ala | Thr | Pro | Leu |
|      | 50        |       |       |     |     | 55        |     |     |     |     | 60        |     | Thr |     |     |
|      | 50        |       |       |     |     | 55        |     |     |     |     | 60        |     |     |     |     |

|     |     |     |      | 85  |     |     |     |     | 90  |     |     |     |     | 95  |     |
|-----|-----|-----|------|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
| Gln | Val | Glu | Val_ | Glu | Leu | Leu | Ser | Arg | G1n | Ser | Gly | Leu | Ser | Gly | Arg |
|     |     |     | 100  |     |     | •   | ٠   | 105 | ٠   |     |     |     | 110 |     |     |
| Gln | Val | Glu | Arg  | Trp | Phe | Arg | Arg | Arg | Arg | Asn | Gln | Asp | Arg | Pro | Ser |
|     |     | 115 |      |     |     |     | 120 |     |     |     |     | 125 |     |     |     |
| Leu | Leu | Lys | Lys  | Phe | Arg | Glu | Ala | Ser | Trp | Arg | Phe | Thr | Phe | Tyr | Leu |
|     | 130 |     |      |     |     | 135 |     |     |     |     | 140 |     |     |     |     |
| Ile | Ala | Phe | Ile  | Ala | Gly | Met | Ala | Val | Ile | Val | Asp | Lys | Pro | Trp | Phe |
| 145 |     |     |      |     | 150 |     |     |     |     | 155 |     |     |     |     | 160 |
| Tyr | Asp | Met | Lys  | Lys | Val | Trp | Glu | Gly | Tyr | Pro | Ile | Gln | Ser | Thr | Ile |
|     |     |     |      | 165 |     |     |     |     | 170 |     |     |     |     | 175 |     |
| Pro | Ser | Gln | Tyr  | Trp | Tyr | Tyr | Met | Ile | Glu | Leu | Ser | Phe | Tyr | Trp | Ser |
|     |     |     | 180  |     |     |     |     | 185 |     |     |     |     | 190 |     |     |
| Leu | Leu | Phe | Ser  | Ile | Ala | Ser | Asp | Val | Lys | Arg | Lys | Asp | Phe | Lys | Glu |
|     |     | 195 |      |     |     |     | 200 |     |     |     |     | 205 |     |     |     |
| Gln | Ile | Ile | His  | His | Val | Ala | Thr | Ile | Ile | Leu | Ile | Ser | Phe | Ser | Trp |
|     | 210 |     |      |     |     | 215 |     |     |     |     | 220 |     |     |     |     |
| Phe | Ala | Asn | Tyr  | Ile | Arg | Ala | Gly | Thr | Leu | Ile | Met | Ala | Leu | His | Asp |
| 225 |     |     | •    |     | 230 |     |     |     |     | 235 |     |     |     |     | 240 |
| Ser | Ser | Asp | Tyr  | Leu | Leu | Glu | Ser | Ala | Lys | Met | Phe | Asn | Tyr | Ala | Gly |
|     |     |     |      | 245 |     |     |     |     | 250 |     |     |     |     | 255 |     |
| Trp | Lys | Asn | Thr  | Cys | Asn | Asn | Ile | Phe | Ile | Val | Phe | Ala | Ile | Val | Phe |
|     |     |     | 260  | )   |     |     |     | 265 | ;   |     |     |     | 270 |     |     |
| Ile | Ile | Thr | Arg  | Leu | Val | Ile | Leu | Pro | Phe | Trp | Ile | Leu | His | Cys | Thr |
|     |     | 275 |      |     |     |     | 200 |     |     |     |     | 205 | :   |     |     |

| Leu             | Val   | Tyr   | Pro   | Leu | Glu | Leu | Tyr   | Pro | Ala | Phe  | Phe | Gly | Tyr | Tyr | Phe |
|-----------------|-------|-------|-------|-----|-----|-----|-------|-----|-----|------|-----|-----|-----|-----|-----|
|                 | 290   |       |       |     |     | 295 |       |     |     |      | 300 |     |     |     |     |
| Phe             | Asn   | Ser   | Met   | Met | Gly | Val | Leu   | Gln | Leu | Leu  | His | Ile | Phe | Trp | Ala |
| 305             |       |       |       |     | 310 |     |       |     |     | 315  |     |     |     |     | 320 |
| Tyr             | Leu   | Ile   | Leu   | Arg | Met | Ala | His   | Lys | Phe | Ile  | Thr | Gly | Lys | Leu | Val |
|                 |       |       |       | 325 |     |     |       |     | 330 |      |     |     |     | 335 |     |
| Glu             | Asp   | Glu   | Arg   | Ser | Asp | Arg | Glu   | Glu | Thr | Glu  | Ser | Ser | Glu | Gly | Glu |
|                 |       |       | 340   |     |     |     |       | 345 |     |      |     |     | 350 |     |     |
| Glu             | Ala   | Ala   | Ala   | Gly | Gly | Gly | Ala   | Lys | Ser | Arg  | Pro | Leu | Ala | Asn | Gly |
|                 |       | 355   |       |     |     |     | 360   |     |     |      |     | 365 |     |     |     |
| His             | Pro   | Ile   | Leu   | Asn | Asn | Asn | His   | Arg | Lys | Asn  | Asp |     |     |     |     |
|                 | 370   |       |       |     |     | 375 |       |     |     |      | 380 |     |     |     |     |
|                 |       |       |       |     |     |     |       |     |     |      |     |     |     |     |     |
| <210            | )> 5  |       |       |     |     |     |       |     |     |      |     |     |     |     |     |
| <b>&lt;21</b> ] | l> 58 | 35    |       |     |     |     |       |     |     |      |     |     |     |     |     |
| <212            | 2> PF | TS    |       |     |     |     |       |     |     |      |     |     |     |     |     |
| <213            | 3> Ho | omo s | sapie | ens |     |     |       |     |     |      |     |     |     |     |     |
| <400            | )> 5  |       |       |     |     |     |       |     |     |      |     |     |     |     |     |
| Met             | Val   | Cys   | Arg   | Glu | Gln | Leu | Ser   | Lys | Asn | Gln  | Val | Lys | Trp | Val | Phe |
| 1               |       |       |       | 5   |     |     |       |     | 10  |      |     |     |     | 15  |     |
| Ala             | Gly   | Ile   | Thr   | Cys | Val | Ser | Val   | Val | Val | Ile  | Ala | Ala | Ile | Val | Leu |
|                 |       |       | 20    |     |     |     |       | 25  |     |      |     |     | 30  |     |     |
| Ala             | Ile   | Thr   | Leu   | Arg | Arg | Pro | Gly   | Cys | Glu | Leu  | Glu | Ala | Cys | Ser | Pro |
|                 |       | 35    |       |     |     |     | 40    |     |     |      |     | 45  |     |     |     |
| Asn             | Ala   | Aen   | Met   | Leu | Asn | Tur | יום ו | Lau | Sor | ī au | C1  | C1- | T1. | Car | A   |

|     | 50    |     |       |       |          | 55   |       |     |       |          | 60   |       |       |     |     |
|-----|-------|-----|-------|-------|----------|------|-------|-----|-------|----------|------|-------|-------|-----|-----|
| Arg | Asp   | Ala | Leu   | Glu   | Val      | Thr  | Trp   | Tyr | His   | Ala      | Ala  | Asn   | Ser   | Lys | Lys |
| 65  |       |     |       |       | 70       |      |       |     |       | 75       |      |       |       |     | 80  |
| Ala | Met   | Thr | Ala   | Ala   | Leu      | Asn  | Ser   | Asn | Ile   | Thr      | Val  | Leu   | Glu   | Ala | Asp |
|     |       |     |       | 85    |          |      |       |     | 90    |          |      |       |       | 95  |     |
| Val | Asn   | Val | Glu   | Gly   | Leu      | Gly  | Thr   | Ala | Asn   | Glu      | Thr  | Gly   | Val   | Pro | Ile |
|     |       |     | 100   |       |          |      |       | 105 |       |          |      |       | 110   |     |     |
| Met | Ala   | His | Pro   | Pro   | Thr      | Ile  | Tyr   | Ser | Asp   | Asn      | Thr  | Leu   | Glu   | Gln | Trp |
|     |       | 115 |       |       |          |      | 120   |     |       |          |      | 125   |       |     |     |
| Leu | Asp   | Ala | Val   | Leu   | Gly      | Ser  | Ser   | Gln | Lys   | Gly      | Ile  | Lys   | Leu   | Asp | Phe |
|     | 130   |     |       |       |          | 135  |       |     |       |          | 140  |       |       |     |     |
| Lys | Asn   | Ile | Lys   | Ala   | Val      | G1y  | Pro   | Ser | Leu   | Asp      | Leu  | Leu   | Arg   | Gln | Leu |
| 145 |       |     |       |       | 150      |      |       |     |       | 155      |      |       |       |     | 160 |
| Thr | Glu   | Glu | Gly   | Lys   | Val      | Arg  | Arg   | Pro | Ile   | Trp      | Ile  | Asn   | Ala   | Asp | Ile |
|     |       |     |       | 165   |          |      |       |     | 170   |          |      |       |       | 175 |     |
| Leu | Lys   | Gly | Pro   | Asn   | Met      | Leu  | Ile   | Ser | Thr   | Glu      | Val  | Asn   | Ala   | Thr | Gln |
|     |       |     | 180   | )     |          |      |       | 185 |       |          |      |       | 190   |     |     |
| Phe | Leu   | Ala | Leu   | ı Val | G1n      | Glu  | Lys   | Tyr | Pro   | Lys      | Ala  | Thr   | Leu   | Ser | Pro |
|     |       | 195 | 5     |       |          |      | 200   |     |       |          |      | 205   | •     |     |     |
| Gly | Trp   | Thr | Thr   | Phe   | y Tyr    | Met  | Ser   | Thr | Ser   | Pro      | Asn  | Arg   | Thr   | Tyr | Thr |
|     | 210   | )   |       |       |          | 215  | 5     |     |       |          | 220  | )     |       |     |     |
| G1n | Ala   | Me1 | t Val | l Glu | ı Lys    | Met  | His   | Glu | l Leu | ı Val    | Gly  | Gly   | v Val | Pro | Gln |
| 225 | 5     |     |       |       | 230      | )    |       |     |       | 235      | 5    |       |       |     | 240 |
| Arg | g Val | Th  | r Pho | e Pro | o Val    | l Ar | g Ser | Ser | Met   | t Val    | l Ar | g Ala | a Ala | Trp | Pro |
|     |       |     |       | 2/19  | <u> </u> |      |       |     | 250   | <b>1</b> |      |       |       | 259 | 5   |

| His | Phe | Ser | Trp | Leu | Leu | Ser | Gln | Ser  | Glu       | Arg | Tyr | Ser | Leu | Thr | Leu |
|-----|-----|-----|-----|-----|-----|-----|-----|------|-----------|-----|-----|-----|-----|-----|-----|
|     |     |     | 260 |     |     |     |     | 265  |           |     |     |     | 270 |     |     |
| Trp | Gln | Ala | Ala | Ser | Asp | Pro | Met | Ser  | Val       | Glu | Asp | Leu | Leu | Tyr | Val |
|     |     | 275 |     |     |     |     | 280 |      |           |     |     | 285 |     |     |     |
| Arg | Asp | Asn | Thr | Ala | Val | His | Gln | Val  | Tyr       | Tyr | Asp | Ile | Phe | Glu | Pro |
|     | 290 |     |     |     |     | 295 |     |      |           |     | 300 |     |     |     |     |
| Leu | Leu | Ser | Gln | Phe | Lys | Gln | Leu | Ala  | Leu       | Asn | Ala | Thr | Arg | Lys | Pro |
| 305 |     |     |     |     | 310 |     |     |      |           | 315 |     |     |     |     | 320 |
| Met | Tyr | Tyr | Thr | Gly | Gly | Ser | Leu | Ile  | Pro       | Leu | Leu | Gln | Leu | Pro | Gly |
|     |     |     |     | 325 |     |     |     |      | 330       |     |     |     |     | 335 |     |
| Asp | Asp | Gly | Leu | Asn | Val | Glu | Trp | Leu  | Val       | Pro | Asp | Val | Gln | Gly | Ser |
|     |     |     | 340 |     |     |     |     | 345  |           |     |     |     | 350 |     |     |
| Gly | Lys | Thr | Ala | Thr | Met | Thr | Leu | Pro  | Asp       | Thr | Glu | Gly | Met | Ile | Leu |
|     |     | 355 |     |     |     |     | 360 |      |           |     |     | 365 |     |     |     |
| Leu | Asn | Thr | Gly | Leu | Glu | Gly | Thr | Val  | Ala       | Glu | Asn | Pro | Val | Pro | Ile |
|     | 370 |     |     |     |     | 375 |     |      |           |     | 380 |     |     |     |     |
| Val | His | Thr | Pro | Ser | Gly | Asn | Ile | Leu  | Thr       | Leu | Glu | Ser | Cys | Leu | Gln |
| 385 |     |     |     |     | 390 |     |     |      |           | 395 |     |     |     |     | 400 |
| Gln | Leu | Ala | Thr | His | Pro | Gly | His | Trp. | Gly       | Ile | His | Leu | G1n | Ile | Ala |
|     |     |     |     | 405 |     |     |     |      | 410       |     |     |     |     | 415 |     |
| Glu | Pro | Ala | Ala | Leu | Arg | Pro | Ser | Leu  | Ala       | Leu | Leu | Ala | Arg | Leu | Ser |
|     |     |     | 420 |     |     |     |     | 425  |           |     |     |     | 430 |     |     |
| Ser | Leu | Gly | Leu | Leu | His | Trp | Pro | Val  | Trp       | Val | Gly | Ala | Lys | Ile | Ser |
|     |     | 435 |     |     |     |     | 440 |      |           |     |     | 445 |     |     |     |
| His | G1y | Ser | Phe | Ser | Val | Pro | Gly | Hi∕s | نر<br>Val | Ala | Glv | Arg | Glu | Leu | Leu |

Thr Ala Val Ala Glu Val Phe Pro His Val Thr Val Ala Pro Gly Trp Pro Glu Glu Val Leu Gly Ser Gly Tyr Arg Glu Gln Leu Leu Thr Asp Met Leu Glu Leu Cys Gln Gly Leu Trp Gln Pro Val Ser Phe Gln Met Gln Ala Met Leu Leu Gly His Ser Thr Ala Gly Ala Ile Gly Arg Leu Leu Ala Ser Ser Pro Arg Ala Thr Val Thr Val Glu His Asn Pro Ala Gly Gly Asp Tyr Ala Ser Val Arg Thr Ala Leu Leu Ala Ala Arg Ala Val Asp Arg Thr Arg Val Tyr Tyr Arg Leu Pro Gln Gly Tyr His Lys Asp Leu Leu Ala His Val Gly Arg Asn 

<210> 6

<211> 331

<212> PRT

<213> Homo sapiens

<400> 6

Met Trp Leu Trp Glu Asp Gln Gly Gly Leu Leu Gly Pro Phe Ser Phe

| Leu | Leu | Leu | Val | Leu | Leu | Leu | Val | Thr | Arg       | Ser        | Pro | Val | Asn | Ala | Cys |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----------|------------|-----|-----|-----|-----|-----|
|     |     |     | 20  |     |     |     |     | 25  |           |            |     |     | 30  |     |     |
| Leu | Leu | Thr | Gly | Ser | Leu | Phe | Val | Leu | Leu       | Arg        | Val | Phe | Ser | Phe | Glu |
|     |     | 35  |     |     |     |     | 40  |     |           |            |     | 45  |     |     |     |
| Pro | Val | Pro | Ser | Cys | Arg | Ala | Leu | Gln | Val       | Leu        | Lys | Pro | Arg | Asp | Arg |
|     | 50  |     |     |     |     | 55  |     |     |           |            | 60  |     |     |     |     |
| Ile | Ser | Ala | Ile | Ala | His | Arg | Gly | Gly | Ser       | His        | Asp | Ala | Pro | Glu | Asn |
| 65  |     |     |     |     | 70  |     |     |     |           | <b>7</b> 5 |     |     |     |     | 80  |
| Thr | Leu | Ala | Ala | Ile | Arg | Gln | Ala | Ala | Lys       | Asn        | Gly | Ala | Thr | Gly | Val |
|     |     |     |     | 85  |     |     |     |     | 90        |            |     |     |     | 95  |     |
| Glu | Leu | Asp | Ile | Glu | Phe | Thr | Ser | Asp | Gly       | Ile        | Pro | Val | Leu | Met | His |
|     |     |     | 100 |     |     |     |     | 105 |           |            |     |     | 110 |     |     |
| Asp | Asn | Thr | Val | Asp | Arg | Thr | Thr | Asp | Gly       | Thr        | Gly | Arg | Leu | Cys | Asp |
|     |     | 115 |     |     |     |     | 120 |     |           |            |     | 125 |     |     |     |
| Leu | Thr | Phe | Glu | Gln | Ile | Arg | Lys | Leu | Asn       | Pro        | Ala | Ala | Asn | His | Arg |
|     | 130 |     |     |     |     | 135 |     |     |           |            | 140 |     |     |     |     |
| Leu | Arg | Asn | Asp | Phe | Pro | Asp | Glu | Lys | Ile       | Pro        | Thr | Leu | Arg | Glu | Ala |
| 145 |     |     |     |     | 150 |     |     |     |           | 155        |     |     |     |     | 160 |
| Val | Ala | Glu | Cys | Leu | Asn | His | Asn | Leu | Thr       | Ile        | Phe | Phe | Asp | Val | Lys |
|     |     |     |     | 165 |     |     |     |     | 170       |            |     |     |     | 175 |     |
| Gly | His | Ala | His | Lys | Ala | Thr | Glu | Ala | Leu       | Lys        | Lys | Met | Tyr | Met | Glu |
|     |     |     | 180 |     |     |     |     | 185 |           |            |     |     | 190 |     |     |
| Phe | Pro | G1n | Leu | Tyr | Asn | Asn | Ser | Val | Val       | Cys        | Ser | Phe | Leu | Pro | Glu |
|     |     | 195 |     |     |     |     | 200 |     |           |            |     | 205 |     |     |     |
| Val | Ile | Tyr | Lys | Met | Arg | Gln | Thr | Asp | ىر<br>Arg | Asp        | Val | Ile | Thr | Ala | Leu |

Thr His Arg Pro Trp Ser Leu Ser His Thr Gly Asp Gly Lys Pro Arg Tyr Asp Thr Phe Trp Lys His Phe Ile Phe Val Met Met Asp Ile Leu Leu Asp Trp Ser Met His Asn Ile Leu Trp Tyr Leu Cys Gly Ile Ser Ala Phe Leu Met Gln Lys Asp Phe Val Ser Pro Ala Tyr Leu Lys Lys Trp Ser Ala Lys Gly Ile Gln Val Val Gly Trp Thr Val Asn Thr Phe Asp Glu Lys Ser Tyr Tyr Glu Ser His Leu Gly Ser Ser Tyr Ile Thr Asp Ser Met Val Glu Asp Cys Glu Pro His Phe ⟨210⟩ 7

<211> 345

<212> PRT

<213> Homo sapiens

<400> 7

Met Ser Pro Glu Glu Trp Thr Tyr Leu Val Val Leu Leu Ile Ser Ile

1 5 10 15

Pro Ile Gly Phe Leu Phe Lys Lys Ala Gly Pro Gly Leu Lys Arg Trp

| Gly | Ala | Ala | Ala | Val | Gly | Leu        | Gly | Leu | Thr       | Leu | Phe | Thr        | Cys | Gly | Pro |
|-----|-----|-----|-----|-----|-----|------------|-----|-----|-----------|-----|-----|------------|-----|-----|-----|
|     |     | 35  |     |     | ٠.  |            | 40  |     |           |     |     | <b>4</b> 5 |     |     |     |
| His | Thr | Leu | His | Ser | Leu | Val        | Thr | Ile | Leu       | Gly | Thr | Trp        | Ala | Leu | Ile |
|     | 50  |     |     |     |     | <b>5</b> 5 |     |     |           |     | 60  |            |     |     |     |
| Gln | Ala | Gln | Pro | Cys | Ser | Cys        | His | Ala | Leu       | Ala | Leu | Ala        | Trp | Thr | Phe |
| 65  |     |     |     |     | 70  |            |     |     |           | 75  |     |            |     |     | 80  |
| Ser | Tyr | Leu | Leu | Phe | Phe | Arg        | Ala | Leu | Ser       | Leu | Leu | Gly        | Leu | Pro | Thr |
|     |     |     |     | 85  |     |            |     |     | 90        |     |     |            |     | 95  |     |
| Pro | Thr | Pro | Phe | Thr | Asn | Ala        | Val | Gln | Leu       | Leu | Leu | Thr        | Leu | Lys | Leu |
|     |     |     | 100 |     |     |            |     | 105 |           |     |     |            | 110 |     |     |
| Val | Ser | Leu | Ala | Ser | Glu | Val        | Gln | Asp | Leu       | His | Leu | Ala        | Gln | Arg | Lys |
|     |     | 115 |     |     |     |            | 120 |     | •         |     |     | 125        |     |     |     |
| Glu | Met | Ala | Ser | Gly | Phe | Ser        | Lys | Gly | Pro       | Thr | Leu | Gly        | Leu | Leu | Pro |
|     | 130 |     |     |     |     | 135        |     |     |           |     | 140 |            |     |     |     |
| Asp | Val | Pro | Ser | Leu | Met | Glu        | Thr | Leu | Ser       | Tyr | Ser | Tyr        | Cys | Tyr | Val |
| 145 |     |     |     |     | 150 |            |     |     |           | 155 |     |            |     |     | 160 |
| Gly | Ile | Met | Thr | G1y | Pro | Phe        | Phe | Arg | Tyr       | Arg | Thr | Tyr        | Leu | Asp | Trp |
|     |     |     |     | 165 |     |            |     |     | 170       |     |     |            |     | 175 |     |
| Leu | Glu | Gln | Pro | Phe | Pro | Gly        | Ala | Val | Pro       | Ser | Leu | Arg        | Pro | Leu | Leu |
|     |     |     | 180 |     |     |            |     | 185 |           |     |     |            | 190 |     |     |
| Arg | Arg | Ala | Trp | Pro | Ala | Pro        | Leu | Phe | Gly       | Leu | Leu | Phe        | Leu | Leu | Ser |
|     |     | 195 |     |     |     |            | 200 |     |           |     |     | 205        |     |     |     |
| Ser | His | Leu | Phe | Pro | Leu | Glu        | Ala | Val | Arg       | Glu | Asp | Ala        | Phe | Tyr | Ala |
|     | 210 |     |     |     |     | 215        |     |     |           |     | 220 |            |     |     |     |
| Arg | Pro | Leu | Pro | Ala | Arg | Leu        | Phe | Tvr | نر<br>Met | He  | Pro | Val        | Phe | Phe | Ala |

225 230 235 240 Phe Arg Met Arg Phe Tyr Val Ala Trp Ile Ala Ala Glu Cys Gly Cys 245 250 255 Ile Ala Ala Gly Phe Gly Ala Tyr Pro Val Ala Ala Lys Ala Arg Ala 270 260 265 Gly Gly Gly Pro Thr Leu Gln Cys Pro Pro Pro Ser Ser Pro Glu Lys 275 280 285 Ala Ala Ser Leu Glu Tyr Asp Tyr Glu Thr Ile Arg Asn Ile Asp Cys 295 300 290 Tyr Ser Thr Asp Phe Cys Val Arg Val Arg Asp Gly Met Arg Tyr Trp 320 310 315 305 Asn Met Thr Val Gln Trp Trp Leu Ala Gln Tyr Ile Tyr Lys Ser Ala 330 335 325 Pro Ala Arg Ser Tyr Val Leu Arg Leu 340 345

<210> 8

<211> 89

<212> PRT

<213> Homo sapiens

20

<400> 8

Met Tyr Met Gln Asp Tyr Trp Arg Thr Trp Leu Lys Gly Leu Arg Gly

1 5 10 15

Phe Phe Phe Val Gly Val Leu Phe Ser Ala Val Ser Ile Ala Ala Phe

25 30

Cys Thr Phe Leu Val Leu Ala Ile Thr Arg His Gln Ser Leu Thr Asp 35 40 45 Pro Thr Ser Tyr Tyr Leu Ser Ser Val Trp Ser Phe Ile Ser Phe Lys 50 55 60 Trp Ala Phe Leu Leu Ser Leu Tyr Ala His Arg Tyr Arg Ala Asp Phe 65 70 75 80 Ala Asp Ile Ser Ile Leu Ser Asp Phe 85 ⟨210⟩ 9 <211> 406 <212> PRT <213> Homo sapiens ⟨400⟩ 9 Met Arg Gly Ser Val Glu Cys Thr Trp Gly Trp Gly His Cys Ala Pro 1 5 10 15 Ser Pro Leu Leu Trp Thr Leu Leu Phe Ala Ala Pro Phe Gly 20 25 30 Leu Leu Gly Glu Lys Thr Arg Gln Val Ser Leu Glu Val Ile Pro Asn 35 40 45 Trp Leu Gly Pro Leu Gln Asn Leu Leu His Ile Arg Ala Val Gly Thr 50 55 60 Asn Ser Thr Leu His Tyr Val Trp Ser Ser Leu Gly Pro Leu Ala Val 65 70 75 Val Met Val Ala Thr Asn Thr Pro His Ser Thr Leu Ser Val Asn Trp

|     |                 |      |               | 85    |       |       |       |     | 90    |     |       |     |                   | 95  |     |
|-----|-----------------|------|---------------|-------|-------|-------|-------|-----|-------|-----|-------|-----|-------------------|-----|-----|
| Ser | Leu             | Leu  | Leu           | Ser   | Pro   | Glu   | Pro   | Asp | Gly   | Gly | Leu   | Met | Va <sub>.</sub> l | Leu | Pro |
|     |                 | •    | 100           |       |       |       |       | 105 |       |     | ٠     |     | 110               | •   |     |
| Lys | Asp             | Ser  | Ile           | Gln   | Phe   | Ser   | Ser   | Ala | Leu   | Val | Phe   | Thr | Arg               | Leu | Leu |
|     |                 | 115  |               |       |       |       | 120   |     |       |     |       | 125 |                   |     |     |
| Glu | Phe             | Asp  | Ser           | Thr   | Asn   | Val   | Ser   | Asp | Thr   | Ala | Ala   | Lys | Pro               | Leu | Gly |
|     | 130             |      |               |       |       | 135   |       |     |       |     | 140   |     |                   |     |     |
| Arg | Pro             | Tyr  | Pro           | Pro   | Tyr   | Ser   | Leu   | Ala | Asp   | Phe | Ser   | Trp | Asn               | Asn | Ile |
| 145 |                 |      |               |       | 150   |       |       |     |       | 155 |       |     |                   |     | 160 |
| Thr | Asp             | Ser  | Leu           | Asp   | Pro   | Ala   | Thr   | Leu | Ser   | Ala | Thr   | Phe | Gln               | Gly | His |
|     |                 |      |               | 165   |       |       |       |     | 170   |     |       |     |                   | 175 |     |
| Pro | Met             | Asn  | Asp           | Pro   | Thr   | Arg   | Thr   | Phe | Ala   | Asn | Gly   | Ser | Leu               | Ala | Phe |
|     |                 |      | 180           |       |       |       |       | 185 |       |     |       |     | 190               |     |     |
| Arg | Val             | Gln  | Ala           | Phe   | Ser   | Arg   | Ser   | Ser | Arg   | Pro | Ala   | Gln | Pro               | Pro | Arg |
|     |                 | 195  | ,             |       |       |       | 200   |     |       |     |       | 205 |                   |     |     |
| Leu | Leu             | His  | Thr           | Ala   | Asp   | Thr   | Cys   | Gln | Leu   | G1u | Val   | Ala | Leu               | Ile | Gly |
|     | 210             | •    |               |       |       | 215   |       |     |       |     | 220   |     |                   |     |     |
| Ala | Ser             | Pro  | Arg           | Gly   | Asn   | Arg   | Ser   | Leu | Phe   | Gly | Leu   | Glu | Val               | Ala | Thr |
| 225 | <b>5</b>        |      | ě             |       | 230   | )     |       |     |       | 235 |       |     |                   |     | 240 |
| Leu | Gly             | Gl:  | n Gly         | Pro   | Asp   | Cys   | Pro   | Ser | Met   | Gln | Glu   | G1n | His               | Ser | Ile |
|     |                 |      |               | 249   | 5     |       |       |     | 250   | •   |       |     |                   | 255 | ,   |
| Asp | As <sub>l</sub> | Gl:  | ц <b>Ту</b> з | r Ala | a Pro | Ala   | a Val | Phe | Gln   | Leu | Asp   | G1r | Leu               | Leu | Trp |
|     |                 |      | 260           | 0     |       |       |       | 265 | 5     |     |       |     | 270               | )   |     |
| Gl  | y Se            | r Le | u Pr          | o Se: | r Gl  | y Pho | e Ala | Glr | ı Çep | Arg | g Pro | Va] | l Ala             | Туг | Ser |
|     |                 | 27   | 5             |       |       |       | 280   | )   |       |     |       | 28  | 5                 |     |     |

| Gln           | Lys   | Pro   | Gly  | Gly | Arg | Glu  | Ser | Ala | Leu      | Pro | Cys | Gln | Ala | Ser | Pro |
|---------------|-------|-------|------|-----|-----|------|-----|-----|----------|-----|-----|-----|-----|-----|-----|
|               | 290   |       |      |     |     | 295  |     |     |          |     | 300 |     |     |     |     |
| Leu           | His   | Pro   | Ala  | Leu | Ala | Tyr  | Ser | Leu | Pro      | Gln | Ser | Pro | Ile | Val | Arg |
| 305           |       |       |      |     | 310 |      |     |     |          | 315 |     |     |     |     | 320 |
| Ala           | Phe   | Phe   | Gly  | Ser | Gln | Asn  | Asn | Phe | Cys      | Ala | Phe | Asn | Leu | Thr | Phe |
|               |       |       |      | 325 |     |      |     |     | 330      |     |     |     |     | 335 |     |
| Gly           | Ala   | Ser   | Thr  | Gly | Pro | G1 y | Tyr | Trp | Asp      | G1n | His | Tyr | Leu | Ser | Trp |
|               |       |       | 340  |     |     |      |     | 345 |          |     |     |     | 350 |     |     |
| Ser           | Met   | Leu   | Leu  | Gly | Val | Gly  | Phe | Pro | Pro      | Val | Asp | Gly | Leu | Ser | Pro |
|               |       | 355   |      |     |     |      | 360 |     |          |     |     | 365 |     |     |     |
| Leu           | Val   | Leu   | Gly  | Ile | Met | Ala  | Val | Ala | Leu      | Gly | Ala | Pro | Gly | Leu | Met |
|               | 370   | •     |      |     |     | 375  |     |     |          |     | 380 |     |     |     |     |
| Leu           | Leu   | Gly   | Gly  | Gly | Leu | Val  | Leu | Leu | Leu      | His | His | Lys | Lys | Tyr | Ser |
| 385           |       |       |      |     | 390 |      |     |     |          | 395 |     |     |     |     | 400 |
| Glu           | Tyr   | Gln   | Ser  | Ile | Asn |      |     |     |          |     |     |     |     |     |     |
|               |       |       |      | 405 |     |      |     |     |          |     |     |     |     |     |     |
|               |       |       |      |     |     |      |     |     |          |     |     |     |     |     |     |
| <210          | )> 10 | )     |      |     |     |      |     |     |          |     |     |     |     |     |     |
| <b>&lt;21</b> | 1> 19 | 92    |      |     |     |      |     | ·   |          |     |     |     | ٠   |     |     |
| <212<br>,     | 2> PI | RT    |      |     |     |      |     |     |          |     |     |     |     |     |     |
| <213          | 3> H  | omo : | sapi | ens |     |      |     |     |          |     |     |     |     |     |     |
| <400          | 0> 10 | 0     |      |     |     |      |     |     |          |     |     |     |     |     |     |
| Met           | Thr   | Ala   | Val  | Gly | Val | Gln  | Ala | Ġln | Arg      | Pro | Leu | Gly | Gln | Arg | Gln |
| 1             |       |       |      | 5   |     |      |     |     | 10       |     |     |     |     | 15  |     |
| Pro           | Arg   | Arg   | Ser  | Phe | Phe | Glu  | Ser | Phe | ر<br>Ile | Arg | Thr | Leu | Ile | Ile | Thr |

|     |     |     | 20  |     |     |     |     | 25  |     |     |     |     | 30  |     |     |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
| Cys | Val | Ala | Leu | Ala | Val | Val | Leu | Ser | Ser | Val | Ser | Ile | Cys | Asp | Gly |
|     |     | 35  |     |     |     | •   | 40  |     |     |     |     | 45  |     | ٠   |     |
| His | Trp | Leu | Leu | Ala | Glu | Asp | Arg | Leu | Phe | Gly | Leu | Trp | His | Phe | Cys |
|     | 50  |     |     |     |     | 55  |     |     |     |     | 60  |     |     |     |     |
| Thr | Thr | Thr | Asn | G1n | Ser | Val | Pro | Ile | Cys | Phe | Arg | Asp | Leu | Gly | Gln |
| 65  |     |     |     |     | 70  |     |     |     |     | 75  |     |     |     |     | 80  |
| Ala | His | Val | Pro | Gly | Leu | Ala | Val | Gly | Met | Gly | Leu | Val | Arg | Ser | Val |
|     |     |     |     | 85  |     |     |     |     | 90  |     |     |     |     | 95  |     |
| Gly | Ala | Leu | Ala | Val | Val | Ala | Ala | Ile | Phe | Gly | Leu | Glu | Phe | Leu | Met |
|     |     |     | 100 |     |     |     |     | 105 |     |     |     |     | 110 |     |     |
| Val | Ser | G1n | Leu | Cys | Glu | Asp | Lys | His | Ser | Gln | Cys | Lys | Trp | Val | Met |
|     |     | 115 |     |     |     |     | 120 |     |     |     |     | 125 |     |     |     |
| Gly | Ser | Ile | Leu | Leu | Leu | Val | Ser | Phe | Val | Leu | Ser | Ser | Gly | Gly | Leu |
|     | 130 |     |     |     |     | 135 |     |     |     |     | 140 |     |     |     |     |
| Leu | Gly | Phe | Val | Ile | Leu | Leu | Arg | Asn | Gln | Val | Thr | Leu | Ile | Gly | Phe |
| 145 |     |     |     |     | 150 |     |     |     |     | 155 |     |     |     |     | 160 |
| Thr | Leu | Met | Phe | Trp | Cys | Glu | Phe | Thr | Ala | Ser | Phe | Leu | Leu | Phe | Leu |
|     |     |     |     | 165 |     |     |     |     | 170 | )   | ٠   |     |     | 175 |     |
| Asn | Ala | Ile | Ser | Gly | Leu | His | Ile | Asn | Ser | Ile | Thr | His | Pro | Trp | Glu |
|     |     |     | 180 | )   |     |     |     | 185 | ;   |     |     |     | 190 | )   |     |

<210> 11

⟨211⟩ 801

<212> DNA

| <213> | Homo | sapiens |
|-------|------|---------|
|       |      | Ouprono |

<400> 11

| atggtgaaga | ttagcttcca | gcccgccgtg | gctggcatca | agggcgacaa | ggctgacaag | 60  |
|------------|------------|------------|------------|------------|------------|-----|
| gcgtcggcgt | cggcccctgc | gccggcctcg | gccaccgaga | tcctgctgac | gccggctagg | 120 |
| gaggagcagc | ccccacaaca | tcgatccaag | agggggagct | cagtgggcgg | cgtgtgctac | 180 |
| ctgtcgatgg | gcatggtcgt | gctgctcatg | ggcctcgtgt | tcgcctctgt | ctacatctac | 240 |
| agatacttct | ttcttgcaca | gctggcccga | gataacttct | tccgctgtgg | tgtgctgtat | 300 |
| gaggactccc | tgtcctccca | ggtccggact | cagatggagc | tggaagagga | tgtgaaaatc | 360 |
| tacctcgacg | agaactacga | gcgcatcaac | gtgcctgtgc | cccagtttgg | cggcggtgac | 420 |
| cctgcagaca | tcatccatga | cttccagcgg | ggtctgactg | cgtaccatga | tatctccctg | 480 |
| gacaagtgct | atgtcatcga | actcaacacc | accattgtgc | tgcccctcg  | caacttctgg | 540 |
| gageteetea | tgaacgtgaa | gagggggacc | tacctgccgc | agacgtacat | catccaggag | 600 |
| gagatggtgg | tcacggagca | tgtcagtgac | aaggaggccc | tggggtcctt | catctaccac | 660 |
| ctgtgcaacg | ggaaagacac | ctaccggctc | cggcgccggg | caacgcggag | gcggatcaac | 720 |
| aagcgtgggg | ccaagaactg | caatgccatc | cgccacttcg | agaacacctt | cgtggtggag | 780 |
| acgctcatct | gcggggtggt | g .        |            |            |            | 80  |

<210> 12

<211> 1257

<212> DNA

<213> Homo sapiens

<400> 12

atgagetgeg egggeegge gggeeetgee eggetegeeg egetegeet getgaeetge 60
ageetgtgge eggeaegge agacaaegeg ageeaggagt actaeaegge geteateaae 120
gtgaeggtge aggageeegg eegeggegee eegeteaegt ttegeatega eegegggege 180

| tacgggcttg | actccccaa    | ggccgaggtc | cgcggccagg | tgctggcgcc | gctgcccctc | 240  |
|------------|--------------|------------|------------|------------|------------|------|
| cacggagttg | ctgatcatct   | gggctgtgat | ccacaaaccç | ggttctttgt | ccctcctaat | 300  |
| atcaaacagt | ggattgcctt   | gctgcagagg | ggaaactgca | cgtttaaaga | gaaaatatca | 360  |
| cgggccgctt | tccacaatgc   | agttgctgta | gtcatctaca | ataataaatc | caaagaggag | 420  |
| ccagttacca | tgactcatcc   | aggcactgga | gatattattg | ctgtcatgat | aacagaattg | 480  |
| aggggtaagg | atattttgag   | ttatctggag | aạaaacatct | ctgtacaaat | gacaatagct | 540  |
| gttggaactc | gaatgccacc   | gaagaacttc | agccgtggct | ctctagtctt | cgtgtcaata | 600  |
| tcctttattg | ttttgatgat   | tatttcttca | gcatggctca | tattctactt | cattcagaag | 660  |
| atcaggtaca | caaatgcacg   | cgacaggaac | cagcgtcgtc | tcggagatgc | agccaagaaa | 720  |
| gccatcagta | aattgacaac   | caggacagta | aagaagggtg | acaaggaaac | tgacccagac | 780  |
| tttgatcatt | gtgcagtctg   | catagagagc | tataagcaga | atgatgtcgt | ccgaattctc | 840  |
| ccctgcaago | atgttttcca   | caaatcctgc | gtggatccct | ggcttagtga | acattgtacc | 900  |
| tgtcctatgt | gcaaacttaa   | tatattgaag | gccctgggaa | ttgtgccgaa | tttgccatgt | 960  |
| actgataacg | g tagcattcga | tatggaaagg | ctcaccagaa | cccaagctgt | taaccgaaga | 1020 |
| tcagccctcg | gegaeetege   | cggcgacaac | tcccttggcc | ttgagccact | tcgaacttcg | 1080 |
| gggatctcad | ctcttcctca   | ggatggggag | ctcactccga | gaacaggaga | aatcaacatt | 1140 |
| gcagtaaca  | a aagaatggtt | tattattgcc | agttttggcc | tcctcagtgc | cctcacactc | 1200 |
| toctacato  | a tcatcagago | cacagetage | ttgaatgota | atgaggtaga | atggttt    | 1257 |

<210> 13

<211> 1245

<212> DNA

<213> Homo sapiens

<400> 13

| CCECEECAEC | agtecceaga | gagaccigii | ticacatgig | giggcatici | tactggagag | 120  |
|------------|------------|------------|------------|------------|------------|------|
| tctggattta | ttggcagtga | aggttttcct | ggagtgtacc | ctccaaatag | caaatgtact | 180  |
| tggaaaatca | cagttcccga | aggaaaagta | gtcgttctca | atttccgatt | catagacctc | 240  |
| gagagtgaca | acctgtgccg | ctatgacttt | gtggatgtgt | acaatggcca | tgccaatggc | 300  |
| cagcgcattg | gccgcttctg | tggcactttc | cggcctggag | cccttgtgtc | cagtggcaac | 360  |
| aagatgatgg | tgcagatgat | ttctgatgcc | aacacagctg | gcaatggctt | catggccatg | 420  |
| ttctccgctg | ctgaaccaaa | cgaaagaggg | gatcagtatt | gtggaggact | ccttgacaga | 480  |
| ccttccggct | cttttaaaac | ccccaactgg | ccagaccggg | attaccctgc | aggagtcact | 540  |
| tgtgtgtggc | acattgtagc | cccaaagaat | cagcttatag | aattaaagtt | tgagaagttt | 600  |
| gatgtggagc | gagataacta | ctgccgatat | gattatgtgg | ctgtgtttaa | tggcggggaa | 660  |
| gtcaacgatg | ctagaagaat | tggaaagtat | tgtggtgata | gtccacctgc | gccaattgtg | 720  |
| tctgagagaa | atgaacttct | tattcagttt | ttatcagact | taagtttaac | tgcagatggg | 780  |
| tttattggtc | actacatatt | caggccaaaa | aaactgccta | caactacaga | acagcctgtc | 840  |
| accaccacat | tccctgtaac | cacgggttta | aaaaccaccg | tggccttgtg | tcaacaaaag | 900  |
| tgtagacgga | cggggactct | ggagggcaat | tattgttcaa | gtgactttgt | attagccggc | 960  |
| actgttatca | caaccatcac | tcgcgatggg | agtttgcacg | ccacagtete | gatcatcaac | 1020 |
| atctacaaag | agggaaattt | ggcgattcag | caggcgggca | agaacatgag | tgccaggctg | 1080 |
| actgtcgtct | gcaagcagtg | ccctctcctc | agaagaggtc | taaattacat | tattatgggc | 1140 |
| caagtaggtg | aagatgggcg | aggcaaaatc | atgccaaaca | gctttatcat | gatgttcaag | 1200 |
| accaagaatc | agaageteet | ggatgcctta | aaaaataagc | aatot      |            | 1245 |

⟨210⟩ 14

⟨211⟩ 1140

<212> DNA

<213> Homo sapiens

⟨400⟩ 14

| atgctccaga | ccttgtatga   | ttacttctgg   | tgggaacgtc   | tgtggctgcc   | tgtgaacttg   | 60   |
|------------|--------------|--------------|--------------|--------------|--------------|------|
| acctgggccg | atctagaaga   | ccgagatgga   | cgtgtctacg   | ccaaagcctc   | agatetetat   | 120  |
| atcacgctgc | ccctggcctt   | gctcttcctc   | atcgttcgat   | acttctttga   | gctgtacgtg   | 180  |
| gctacaccac | tggctgccct   | cttgaacata   | aaggagaaaa   | ctcggctgcg   | ggcacctccc   | 240  |
| aacgccacct | tggaacattt   | ctacctgacc   | agtggcaagc   | agcccaagca   | ggtggaagta   | 300  |
| gagettttgt | cccggcagag   | cgggctctct   | ggccgccagg   | tagagcgttg   | gttccgtcgc   | 360  |
| cgccgcaacc | aggaccggcc   | cagtctcctc   | aagaagttcc   | gagaagccag   | ctggagattc   | 420  |
| acattttacc | tgattgcctt   | cattgccggc   | atggccgtca   | ttgtggataa   | accctggttc   | 480  |
| tatgacatga | agaaagtttg   | ggagggatat   | cccatacaga   | gcactatccc   | ttcccagtat   | 540  |
| tggtactaca | tgattgaact   | ttccttctac   | tggtccctgc   | tcttcagcat   | tgcctctgat   | 600  |
| gtcaagcgaa | aggatttcaa   | ggaacagatc   | atccaccatg   | tggccaccat   | cattctcatc   | 660  |
| agcttttcct | ggtttgccaa   | ttacatccga   | gctgggactc   | taatcatggc   | tctgcatgac   | 720  |
| tcttccgatt | acctgctgga   | gtcagccaag   | atgtttaact   | acgcgggatg   | gaagaacacc   | 780  |
| tgcaacaaca | tcttcatcgt   | cttcgccatt   | gtttttatca   | tcacccgact   | ggtcatcctg   | 840  |
| cccttctgga | a tcctgcattg | caccctggtg   | tacccactgg   | agctctatcc   | tgccttcttt   | 900  |
| ggctattact | tcttcaattc   | catgatggga   | gttctacago   | tgctgcatat   | cttctgggcc   | 960  |
| tacctcatt  | t tgcgcatggo | ccacaagtto   | ataactggaa   | a agctggtaga | agatgaacgc   | 1020 |
| agtgaccgg  | g aagaaacaga | a gagctcagag | g ggggaggagg | g ctgcagctgg | gggaggagca   | 1080 |
| aagagccgg  | c ccctagccaa | a tggccaccc  | atcctcaata   | a acaaccatce | g taagaatgac | 1140 |

<210> 15

<211> 1755

<212> DNA

<213≻ Homo sapiens

⟨400⟩ 15

| 60   | cggcattacc | gggtgtttgc | caggtcaagt      | atcaaagaat | gggagcagtt | atggtctgca |
|------|------------|------------|-----------------|------------|------------|------------|
| 120  | gcggccaggc | tcaccctgcg | gtccttgcca      | tgccgcaata | tggtggtcat | tgtgtgtctg |
| 180  | gagcctgggc | actacctgct | gacatgctgg      | ccctgatgcc | aggcctgcag | tgtgagctgg |
| 240  | cagcaagaaa | acgcagccaa | acctggtacc      | cttggaggtc | ggcgagatgc | cagatcagcc |
| 300  | caatgtagaa | aggctgacgt | acagtcctgg      | cagcaacatc | ctgccctgaa | gccatgacag |
| 360  | cactatctac | cacacccccc | cccatcatgg      | gacaggagtt | cagccaatga | gggctcggca |
| 420  | aaagggcatc | gctcttccca | gctgtgctgg      | gtggctggac | cactggagca | agtgacaaca |
| 480  | gcggcagctg | tggacctcct | ggccctccc       | caaggcagtg | tcaagaacat | aaactggact |
| 540  | aaagggcccc | ctgacatctt | tggatcaacg      | gcggcccata | gcaaagtccg | acagaggaag |
| 600  | ccaggagaag | tggccctggt | acacagttcc      | ggtcaatgcc | tctcaactga | aacatgctca |
| 660  | gtccccaaac | acatgtccac | accaccttct      | tccaggctgg | ctaccctatc | tatcccaagg |
| 720  | agtgccccag | tggtgggagg | atgcacgagc      | ggtggagaag | cccaagccat | aggacgtaca |
| 780  | cttcagctgg | cctggcccca | gtgcgggctg      | gtcttccatg | tccctgtacg | agggtcacct |
| 840  | ggaccccatg | aggctgcctc | acgctgtggc      | gtacagcctg | aatctgagag | ctgctgagcc |
| 900  | ctactatgac | tccaccaagt | aacactgctg      | cgtccgggat | atctgctcta | tcggtggaag |
| 960  | acggaaacca | tgaatgccac | cagctggcct      | acagttcaag | ctctcctgtc | atctttgagc |
| 1020 | tgacggtctg | tgcctgggga | cttctccagc      | cctgatccct | caggaggcag | atgtactaca |
| 1080 | aatgaccctc | aaacagcaac | ggcagcggta      | tgacgtccag | ggctggttcc | aatgtggagt |
| 1140 | ggctgaaaac | agggaactgt | actggcctcg      | cctgctgaac | aaggcatgat | ccagacacag |
| 1200 | ctgcctgcag | cgctggagtc | aacatcctga      | tccaagtggc | ttgttcatac | cccgtgccca |
| 1260 | gcccgcagcc | aaatagcgga | atccatttgc      | acactggggc | cacatcccgg | cagctggcca |
| 1320 | gcattggcct | ttggcctctt | ctctccagcc      | gctggcacgc | ccctggcctt | ctccggccat |
| 1380 | tgtggctggc | tccccggcca |                 | ctcccacggg | gggccaaaat | gtgtgggttg |
| 1440 | accaggctgg | tgactgtggc | شر<br>ttccccacg | ggctgaggtc | ttacagctgt | agagagetge |

cetgaggagg tgetgggcag tggetacagg gaacagetge teacagatat getagagttg 1500
tgceagggge tetggeaace tgtgteette cagatgcagg ceatgetget gggecacage 1560
acagetggag ceataggeag getgetggea teeteecee gggecacegt caeagtggag 1620
caeaaceeag etgggggega etatgeetet gtgaggacag cattgetgge agetaggget 1680
gtggacagga eeegagteta etacaggeta eeecaggget aceacaagga ettgetgget 1740
catgttggta gaaac 1755

<210> 16

**<211> 993** 

<212> DNA

<213> Homo sapiens

<400> 16

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| atgcataata | tcttgtggta | cctgtgtgga | atttcagctt | tcctcatgca | aaaggatttt | 840 |
|------------|------------|------------|------------|------------|------------|-----|
| gtatccccgg | cctacttgaa | gaagtggtca | gctaaaggaa | tccaggttgt | tggttggact | 900 |
| gttaatacct | ttgatgaaaa | gagttactac | gaatcccatc | ttggttccag | ctatatcact | 960 |
| gacagcatgg | tagaagactg | cgaacctcac | ttc        |            |            | 993 |

⟨210⟩ 17

⟨211⟩ 1035

<212> DNA

<213> Homo sapiens

<400> 17

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300

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| 8 | acatcgact  | gctacagcac  | agatttctgc   | gtgcgggtgc  | gcgatggcat   | gcggtactgg | 960  |
|---|------------|-------------|--------------|-------------|--------------|------------|------|
| 8 | acatgacgg  | tgcagtggtg  | gctggcgcag   | tatatctaca  | agagcgcacc   | tgcccgttcc | 1020 |
| 1 | tatgtcctgc | gcctt       |              | •           |              |            | 1035 |
|   |            |             |              |             |              |            |      |
| • | (210> 18   |             |              |             |              |            |      |
| • | <211> 267  |             |              |             |              |            |      |
| , | <212> DNA  |             |              |             |              |            |      |
| , | <213> Homo | sapiens     |              |             |              |            |      |
|   | <400> 18   |             |              |             |              |            |      |
|   | atgtacatgc | aagattattg  | gaggacctgg   | ctcaaggggc  | tgcgcggctt   | cttcttcgtg | 60   |
|   | ggcgtcctct | tctcggccgt  | ctccatcgct   | gccttctgca  | ccttcctcgt   | gctggccatc | 120  |
|   | acccggcatc | agagcctcac  | agaccccacc   | agctactacc  | tctccagcgt   | ctggagcttc | 180  |
|   | atttccttca | agtgggcctt  | cctgctcagc   | ctctatgccc  | accgctaccg   | ggctgacttt | 240  |
|   | gctgacatca | gcatcctcag  | cgatttc      |             |              |            | 267  |
|   |            |             |              |             |              |            |      |
|   | <210> 19   |             |              |             |              |            |      |
|   | <211> 1218 | :           |              |             |              |            |      |
|   | <212> DNA  |             |              |             |              |            |      |
|   | <213> Homo | sapiens     |              |             |              | •          |      |
|   | <400> 19   |             |              |             |              |            |      |
|   | atgcgcggct | ctgtggagtg  | g cacctgggg1 | tgggggcact  | t gtgccccag  | cccctgctc  | 6    |
|   | ctttggacto | tacttctgt1  | t tgcagccca  | tttggcctg   | c tgggggagaa | gacccgccag | 12   |
|   | gtgtctctgg | g aggtcatcc | c taactggct; | g ggccccctg | c agaacctgc1 | tcatatacgg | 18   |
|   | gcagtgggca | a ccaattcca | c actgcacta  | t gtgtggagc | a gcctggggc  | tctggcagtg | 24   |

gtaatggtgg ccaccaacac cccccacagc accctgagcg tcaactggag cctcctgcta

| tcccctgagc | ccgatggggg | cctgatggtg | ctccctaagg | acagcattca | gttttcttct | 360  |
|------------|------------|------------|------------|------------|------------|------|
| gcccttgttt | ttaccagget | gcttgagttt | gacagcacca | acgtgtccga | tacggcagca | 420  |
| aagcctttgg | gaagaccata | tcctccatac | tccttggccg | atttctcttg | gaacaacatc | 480  |
| actgattcat | tggatcctgc | caccctgagt | gccacatttc | aaggccaccc | catgaacgac | 540  |
| cctaccagga | cttttgccaa | tggcagcctg | gccttcaggg | tccaggcctt | ttccaggtcc | 600  |
| agccgaccag | cccaaccccc | tcgcctcctg | cacacagcag | acacctgtca | gctagaggtg | 660  |
| gccctgattg | gagcctctcc | ccggggaaac | cgttccctgt | ttgggctgga | ggtagccaca | 720  |
| ttgggccagg | gccctgactg | ccctcaatg  | caggagcagc | actccatcga | cgatgaatat | 780  |
| gcaccggccg | tcttccagtt | ggaccagcta | ctgtggggct | ccctcccatc | aggctttgca | 840  |
| cagtggcgac | cagtggctta | ctcccagaag | ccggggggcc | gagaatcagc | cctgccctgc | 900  |
| caagcttccc | ctcttcatcc | tgccttagca | tactctcttc | cccagtcacc | cattgtccga | 960  |
| gccttctttg | ggtcccagaa | taacttctgt | gccttcaatc | tgacgttcgg | ggcttccaca | 1020 |
| ggccctggct | attgggacca | acactacctc | agctggtcga | tgctcctggg | tgtgggcttc | 1080 |
| cctccagtgg | acggcttgtc | cccactagtc | ctgggcatca | tggcagtggc | cctgggtgcc | 1140 |
| ccagggctca | tgctgctagg | gggcggcttg | gttctgctgc | tgcaccacaa | gaagtactca | 1200 |
| gagtaccagt | ccataaat   |            |            |            |            | 1218 |

⟨210⟩ 20

<211> 576

<212> DNA

<213> Homo sapiens

<400> 20

| atgactgccg tcggcgtgca g | gcccagagg  | cctttgggcc       | aaaggcagcc | ccgccggtcc | 60  |
|-------------------------|------------|------------------|------------|------------|-----|
| ttctttgaat ccttcatccg g | gacceteate | atcacgtgtg       | tggccctggc | tgtggtcctg | 120 |
| tcctcggtct ccatttgtga t | tgggcactgg | سر<br>ctcctggctg | aggaccgcct | cttcgggctc | 180 |

| tggcacttct į            | gcaccaccac  | caaccagagt  | gtgccgatct  | gcttcagaga  | cctgggccag | 240 |
|-------------------------|-------------|-------------|-------------|-------------|------------|-----|
| gcccatgtgc              | ccgggctggc  | cgtgggcatg  | ggcctggtac  | gcagcgtggg  | cgccttggcc | 300 |
| gtggtggccg              | ccatttttgg  | cctggagttc  | ctcatggtgt  | cccagttgtg  | cgaggacaaa | 360 |
| cactcacagt              | gcaagtgggt  | catgggttcc  | atcctcctcc  | tggtgtcttt  | cgtcctctcc | 420 |
| tccggcgggc              | tcctgggttt  | tgtgatcctc  | ctcaggaacc  | aagtcacact  | catcggcttc | 480 |
| accctaatgt              | tttggtgcga  | attcactgcc  | tccttcctcc  | tcttcctgaa  | cgccatcagc | 540 |
| ggccttcaca              | tcaacagcat  | cacccatccc  | tgggaa      |             |            | 576 |
|                         |             |             |             |             |            |     |
| <210> 21                |             |             |             |             |            |     |
| <b>&lt;211&gt; 2042</b> |             |             |             |             |            |     |
| <212> DNA               |             |             |             |             |            |     |
| <213> Homo              | sapiens     |             |             |             |            |     |
| <220>                   |             |             |             |             |            |     |
| <221> CDS               |             |             |             |             |            |     |
| <222> (91).             | (894)       |             |             |             |            |     |
| <b>&lt;400&gt;</b> 21   |             |             |             |             |            |     |
| tccggtgcct              | gcagagctcg  | gagcggcgga  | ggcagagacc  | gaggctgcac  | cggcagaggc | 60  |
| tgcggggcgg              | acgcgcgggc  | cggcgcagcc  | atg gtg aa  | g att agc t | tc cag     | 111 |
|                         |             |             | Met Val Ly  | s Ile Ser P | he Gln     |     |
|                         |             |             | 1           | 5           |            |     |
| ccc gcc gtg             | g gct ggc a | atc aag ggc | gac aag gct | gac aag go  | g tcg gcg  | 159 |
| Pro Ala Val             | Ala Gly     | lle Lys Gly | Asp Lys Ala | Asp Lys Al  | a Ser Ala  |     |
| 10                      | )           | 15          |             | 20          |            |     |
| tcg gcc cci             | t gcg ccg i | gcc tcg gcc | acc gag ato | ctg ctg ac  | g ccg gct  | 207 |

Ser Ala Pro Ala Pro Ala Ser Ala Thr Glu Ile Leu Leu Thr Pro Ala

|     | 25  |     |            |     |            | 30  |     |     |           |     | 35  |     |     |     |     |     |
|-----|-----|-----|------------|-----|------------|-----|-----|-----|-----------|-----|-----|-----|-----|-----|-----|-----|
| agg | gag | gag | cag        | ccc | cca        | caa | cat | cga | tcc       | aag | agg | ggg | agc | tca | gtg | 255 |
| Arg | Glu | Glu | Gln        | Pro | Pro        | Gln | His | Arg | Ser       | Lys | Arg | Gly | Ser | Ser | Val | ٠   |
| 40  |     |     |            |     | <b>4</b> 5 |     |     |     | •         | 50  |     |     |     |     | 55  |     |
| ggc | ggc | gtg | tgc        | tac | ctg        | tcg | atg | ggc | atg       | gtc | gtg | ctg | ctc | atg | ggc | 303 |
| Gly | Gly | Val | Cys        | Tyr | Leu        | Ser | Met | Gly | Met       | Val | Val | Leu | Leu | Met | Gly |     |
|     |     |     |            | 60  |            |     |     |     | 65        |     |     |     |     | 70  |     |     |
| ctc | gtg | ttc | gcc        | tct | gtc        | tac | atc | tac | aga       | tac | ttc | ttt | ctt | gca | cag | 351 |
| Leu | Val | Phe | Ala        | Ser | Val        | Tyr | Ile | Tyr | Arg       | Tyr | Phe | Phe | Leu | Ala | Gln |     |
|     |     |     | <b>7</b> 5 |     |            |     |     | 80  |           |     |     |     | 85  |     |     |     |
| ctg | gcc | cga | gat        | aac | ttc        | ttc | cgc | tgt | ggt       | gtg | ctg | tat | gag | gac | tcc | 399 |
| Leu | Ala | Arg | Asp        | Asn | Phe        | Phe | Arg | Cys | Gly       | Val | Leu | Tyr | Glu | Asp | Ser |     |
|     |     | 90  |            |     |            |     | 95  |     |           |     |     | 100 |     |     |     |     |
|     |     |     |            |     | cgg        |     |     |     |           |     |     |     |     |     |     | 447 |
| Leu |     | Ser | Gln        | Val | Arg        | Thr | Gln | Met | Glu       | Leu | Glu | Glu | Asp | Val | Lys |     |
|     | 105 |     |            |     |            | 110 |     |     |           |     | 115 |     |     |     |     |     |
|     |     |     |            |     | aac        |     |     |     |           |     |     |     |     |     |     | 495 |
|     | Tyr | Leu | Asp        | Glu | Asn        | Tyr | Glu | Arg | Ile       | Asn | Val | Pro | Val | Pro | G1n |     |
| 120 |     |     |            |     | 125        |     |     |     |           | 130 |     |     |     |     | 135 |     |
|     |     |     |            |     | cct        |     |     |     |           |     |     |     |     |     |     | 543 |
| Phe | Gly | Gly | Gly        |     | Pro        | Ala | Asp | Ile | Ile       | His | Asp | Phe | Gln | Arg | Gly |     |
|     |     |     |            | 140 |            |     |     |     | 145       |     |     |     |     | 150 |     |     |
|     |     |     |            |     | gat        |     |     |     |           |     |     |     |     |     |     | 591 |
| Leu | Thr | Ala |            | His | Asp        | Ile | Ser |     | Asp<br>نر | Lys | Cys | Tyr |     |     | Glu |     |
|     |     |     | 155        |     |            |     |     | 160 |           |     |     |     | 165 |     |     |     |

| ctc         | aac  | acc  | acc   | att  | gtg   | ctg  | ccc  | cct   | cgc  | aac  | ttc   | tgg   | gag         | ctc  | ctc    | 639  |
|-------------|------|------|-------|------|-------|------|------|-------|------|------|-------|-------|-------------|------|--------|------|
| Leu         | Asn  | Thr  | Thr   | Ile  | Val   | Leu  | Pro  | Pro   | Arg  | Asn  | Phe   | Trp   | Glu         | Leu  | Leu    |      |
|             |      | 170  |       |      | •     |      | 175  |       |      |      |       | 180   | .•          |      | •      |      |
| atg         | aac  | gtg  | aag   | agg  | ggg   | acc  | tac  | ctg   | ccg  | cag  | acg   | tac   | atc         | atc  | cag    | 687  |
| Met         | Asn  | Val  | Lys   | Arg  | Gly   | Thr  | Tyr  | Leu   | Pro  | Gln  | Thr   | Tyr   | Ile         | Ile  | G1n    |      |
|             | 185  |      |       |      |       | 190  |      |       |      |      | 195   |       |             |      |        |      |
| gag         | gag  | atg  | gtg   | gtc  | acg   | gag  | cat  | gtc   | agt  | gac  | aag   | gag   | gcc         | ctg  | ggg    | 735  |
|             |      |      |       |      |       |      |      |       |      |      |       |       |             | Leu  | _      |      |
| 200         |      |      |       |      | 205   |      |      |       |      | 210  | •     |       |             |      | 215    |      |
|             | ttc  | atc  | tac   | cac  |       | tøc  | aac  | 999   | ลลล  |      | acc   | tac   | <b>ന</b> മമ | ctc  |        | 783  |
|             |      |      |       |      |       |      |      |       |      |      |       |       |             | Leu  |        | 100  |
| ger.        | rne  | 116  | 1 9 1 |      | Leu   | Cys  | nSii | GIY   | -    | nsp  | 1111  | Iyı   | VI B        |      | vid    |      |
|             |      | •    |       | 220  |       |      |      |       | 225  |      |       |       |             | 230  |        |      |
| cgc         | cgg  | gca  | acg   | cgg  | agg   | cgg  | atc  | aac   | aag  | cgt  | ggg   | gcc   | aag         | aac  | tgc    | 831  |
| Arg         | Arg  | Ala  | Thr   | Arg  | Arg   | Arg  | Ile  | Asn   | Lys  | Arg  | Gly   | Ala   | Lys         | Asn  | Cys    |      |
|             |      |      | 235   |      |       |      |      | 240   |      |      |       |       | 245         |      |        |      |
| aat         | gcc  | atc  | cgc   | cac  | ttc   | gag  | aac  | acc   | ttc  | gtg  | gtg   | gag   | acg         | ctc  | atc    | 879  |
| Asn         | Ala  | Ile  | Arg   | His  | Phe   | Glu  | Asn  | Thr   | Phe  | Val  | Val   | Glu   | Thr         | Leu  | Ile    |      |
|             |      | 250  |       |      |       |      | 255  |       |      |      |       | 260   | ı           |      |        |      |
| tgc         | ggg  | gtg  | gtg   | tga  | ggcc  | ctc  | ctcc | ccca  | ga a | cccc | ctgc  | c gt  | gtto        | ctc  |        | 930  |
| Cys         | Gly  | Val  | Val   |      |       |      |      |       |      |      |       |       |             |      |        |      |
|             | 265  | ,    |       |      |       |      |      |       |      |      |       |       | •           |      |        |      |
| ttt         | tctt | ctt  | tccg  | gctg | ct c  | tctg | gccc | t cc  | tcct | tccc | cct   | gctt  | agc         | ttgt | actttg | 990  |
| gac         | gcgt | ttc  | tata  | gagg | gtg a | catg | tctc | t cc  | atto | ctct | cca   | acco  | tgc         | ccac | ctccct | 1050 |
| gta         | ccag | gagc | tgtg  | atct | ct c  | ggtg | gggg | g co  | cato | tctg | ctg   | acci  | ggg         | tgtg | gcggag | 1110 |
| <b>0</b> 02 | 0200 | rcga | tect  | geaa | nag t | etti | tete | rt σt | CCCS | ctgt | : ctt | ะฮลลเ | nctø        | ggco | tgccaa | 1170 |

<400≻ 22

46

#### 34 /307

| agcctgggcc | cacagctgca | ccggcagccc | aaggggaagg | accggttggg | ggagccgggc | 1230 |
|------------|------------|------------|------------|------------|------------|------|
| atgtgaggcc | ctgggcaagg | ggatggggct | gtgggggcgg | ggcggcatgg | gcttcagaag | 1290 |
| tatctgcaca | attagaaaag | tcctcagaag | cttttcttg  | gagggtacac | tttcttcact | 1350 |
| gtccctattc | ctagacctgg | ggcttgagct | gaggatggga | cgatgtgccc | agggagggac | 1410 |
| ccaccagagc | acaagagaag | gtggctacct | gggggtgtcc | cagggactct | gtcagtgcct | 1470 |
| tcagcccacc | agcaggagct | tggagtttgg | ggagtgggga | tgagtccgtc | aagcacaact | 1530 |
| gttctctgag | tggaaccaaa | gaagcaagga | gctaggaccc | ccagtcctgc | ccccaggag  | 1590 |
| cacaagcagg | gtccctcag  | tcaaggcagt | gggatgggcg | gctgaggaac | ggggcaggca | 1650 |
| aggtcactgc | tcagtcacgt | ccacggggga | cgagccgtgg | gttctgctga | gtaggtggag | 1710 |
| ctcattgctt | tctccaagct | tggaactgtt | ttgaaagata | acacagaggg | aaagggagag | 1770 |
| ccacctggta | cttgtccacc | ctgcctcctc | tgttctgaaa | ttccatcccc | ctcagcttag | 1830 |
| gggaatgcac | ctttttccct | ttccttctca | cttttgcatg | ttttactga  | tcattcgata | 1890 |
| tgctaaccgt | tctcagccct | gagccttgga | gaggagggct | gtaacgcctt | cagtcagtct | 1950 |
| ctggggatga | aactcttaaa | tgctttgtat | attttctcaa | ttagatctct | tttcagaagt | 2010 |
| gtctatagaa | caataaaaat | cttttacttc | tg         |            |            | 2042 |
| <210> 22   |            |            |            |            |            |      |
| <211> 1433 |            |            |            |            |            |      |
| <212> DNA  |            |            |            |            |            |      |
| <213> Homo | sapiens    |            |            | •          |            |      |
| ⟨220⟩      |            |            |            |            |            |      |
| <221> CDS  |            |            |            |            |            |      |
| ⟨222⟩ (5)  | . (1264)   |            |            |            |            |      |

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|     | 1   | •     |       |     | 5      | ,   |     |     |     | 10  | )   |     |     |       |          |     |
|-----|-----|-------|-------|-----|--------|-----|-----|-----|-----|-----|-----|-----|-----|-------|----------|-----|
| ctc | gcc | ctg   | ctg   | acc | tgc    | agc | ctg | tgg | ccg | gca | cgg | gca | gac | aac   | gcg      | 94  |
| Leu | Ala | Leu   | Leu   | Thr | Cys    | Ser | Leu | Trp | Pro | Ala | Arg | Ala | Asp | Asn   | Ala      |     |
| 15  |     |       |       |     | 20     |     |     |     |     | 25  |     |     |     |       | 30       |     |
| agc | cag | gag   | tac   | tac | acg    | gcg | ctc | atc | aac | gtg | acg | gtg | cag | gag   | ccc      | 142 |
| Ser | Gln | Glu   | Tyr   | Tyr | Thr    | Ala | Leu | Ile | Asn | Val | Thr | Val | G1n | Glu   | Pro      |     |
|     |     |       |       | 35  |        |     |     |     | 40  |     |     |     |     | 45    |          |     |
| ggc | cgc | ggc   | gcc   | ccg | ctc    | acg | ttt | cgc | atc | gac | cgc | ggg | cgc | tac   | ggg      | 190 |
| Gly | Arg | Gly   | Ala   | Pro | Leu    | Thr | Phe | Arg | Ile | Asp | Arg | Gly | Arg | Tyr   | Gly      |     |
|     |     |       | 50    |     |        |     |     | 55  |     |     |     |     | 60  |       |          |     |
| ctt | gac | tcc   | ccc   | aag | gcc    | gag | gtc | cgc | ggc | cag | gtg | ctg | gcg | ccg   | ctg      | 238 |
| Leu | Asp | Ser   | Pro   | Lys | Ala    | Glu | Val | Arg | Gly | G1n | Val | Leu | Ala | Pro   | Leu      |     |
|     |     | 65    |       |     |        |     | 70  |     |     |     |     | 75  |     |       |          |     |
| ccc | ctc | cac   | gga   | gtt | gct    | gat | cat | ctg | ggc | tgt | gat | cca | caa | acc   | cgg      | 286 |
| Pro | Leu | His   | Gly   | Val | Ala    | Asp | His | Leu | Gly | Cys | Asp | Pro | G1n | Thr   | Arg      |     |
|     | 80  |       |       |     |        | 85  |     |     |     |     | 90  |     |     |       |          |     |
| ttc | ttt | gto   | cct   | cct | aat    | atc | aaa | cag | tgg | att | gcc | ttg | ctg | cag   | agg      | 334 |
| Phe | Phe | Val   | Pro   | Pro | Asn    | Ile | Lys | Gln | Trp | Ile | Ala | Leu | Leu | Gln   | Arg      |     |
| 95  |     |       |       |     | 100    |     |     | •   |     | 105 |     |     |     |       | 110      |     |
| gga | aac | tgo   | acg   | ttt | aaa    | gag | aaa | ata | tca | cgg | gcc | gct | ttc | cac   | aat      | 382 |
| Gly | Asn | Cys   | Thr   | Phe | Lys    | Glu | Lys | Ile | Ser | Arg | Ala | Ala | Phe | His   | . Asn    |     |
|     |     |       |       | 115 | ,<br>1 |     |     |     | 120 | )   |     |     |     | 125   | <b>;</b> |     |
| gca | gtt | gct   | gta   | gto | ato    | tac | aat | aat | aaa | tco | aaa | gag | gag | g cca | gtt      | 430 |
| Ala | Va] | l Ala | a Val | Val | Ile    | Yyr | Asn | Asn | Lys | Ser | Lys | Glu | Glu | ı Pro | Val      |     |
|     |     |       | 130   | )   |        |     |     | 135 | 5   |     |     |     | 140 | )     |          |     |

| acc | atg | act | cat | cca | ggc | act | gga | gat | att      | att | gct | gtc | atg | ata | aca | 478 |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|----------|-----|-----|-----|-----|-----|-----|-----|
| Thr | Met | Thr | His | Pro | Gly | Thr | Gly | Asp | Ile      | Ile | Ala | Val | Met | Ile | Thr |     |
|     |     | 145 |     | ٠   |     |     | 150 |     |          |     |     | 155 |     |     | ·   |     |
| gaa | ttg | agg | ggt | aag | gat | att | ttg | agt | tat      | ctg | gag | aaa | aac | atc | tct | 526 |
| Glu | Leu | Arg | Gly | Lys | Asp | Ile | Leu | Ser | Tyr      | Leu | Glu | Lys | Asn | Ile | Ser |     |
|     | 160 |     |     |     |     | 165 |     |     |          |     | 170 |     |     |     |     |     |
| gta | caa | atg | aca | ata | gct | gtt | gga | act | cga      | atg | cca | ccg | aag | aac | ttc | 574 |
| Val | Gln | Met | Thr | Ile | Ala | Val | Gly | Thr | Arg      | Met | Pro | Pro | Lys | Asn | Phe |     |
| 175 |     |     |     |     | 180 |     |     |     |          | 185 |     |     |     |     | 190 |     |
| agc | cgt | ggc | tct | cta | gtc | ttc | gtg | tca | ata      | tcc | ttt | att | gtt | ttg | atg | 622 |
| Ser | Arg | Gly | Ser | Leu | Val | Phe | Val | Ser | Ile      | Ser | Phe | Ile | Val | Leu | Met |     |
|     |     |     |     | 195 |     |     |     |     | 200      |     |     |     |     | 205 |     |     |
| att | att | tct | tca | gca | tgg | ctc | ata | ttc | tac      | ttc | att | cag | aag | atc | agg | 670 |
| Ile | Ile | Ser | Ser | Ala | Trp | Leu | Ile | Phe | Tyr      | Phe | Ile | Gln | Lys | Ile | Arg |     |
|     |     |     | 210 |     |     |     |     | 215 |          |     |     |     | 220 |     |     |     |
| tac | aca | aat | gca | cgc | gac | agg | aac | cag | cgt      | cgt | ctc | gga | gat | gca | gcc | 718 |
| Tyr | Thr | Asn | Ala | Arg | Asp | Arg | Asn | G1n | Arg      | Arg | Leu | Gly | Asp | Ala | Ala |     |
|     |     | 225 |     |     |     |     | 230 |     |          |     |     | 235 |     |     |     |     |
| aag | aaa | gcc | atc | agt | aaa | ttg | aca | acc | agg      | aca | gta | aag | aag | ggt | gac | 766 |
| Lys | Lys | Ala | Ile | Ser | Lys | Leu | Thr | Thr | Arg      | Thr | Val | Lys | Lys | Gly | Asp |     |
|     | 240 |     |     |     |     | 245 |     |     |          |     | 250 |     |     |     |     |     |
| aag | gaa | act | gac | cca | gac | ttt | gat | cat | tgt      | gca | gtc | tgc | ata | gag | agc | 814 |
| Lys | Glu | Thr | Asp | Pro | Asp | Phe | Asp | His | Cys      | Ala | Val | Cys | Ile | Glu | Ser |     |
| 255 |     |     |     |     | 260 |     |     |     |          | 265 |     |     |     |     | 270 |     |
| tat | aag | cag | aat | gat | gtc | gtc | cga | att | ۔<br>ctc | ccc | tgc | aag | cat | gtt | ttc | 862 |

| Tyr | Lys  | Gln   | Asn   | Asp   | Val   | Val   | Arg   | Ile   | Leu   | Pro   | Cys  | Lys   | His  | Val   | Phe   |      |
|-----|------|-------|-------|-------|-------|-------|-------|-------|-------|-------|------|-------|------|-------|-------|------|
|     |      |       |       | 275   |       |       |       | •     | 280   | •     |      |       |      | 285   |       |      |
| các | aaa  | tcc   | tgc   | gtg   | gat   | ccc   | tgg   | ctt   | agt   | gaa   | cat  | tgt   | acc  | tgt   | cct   | 910  |
| His | Lys  | Ser   | Cys   | Val   | Asp   | Pro   | Trp   | Leu   | Ser   | Glu   | His  | Cys   | Thr  | Cys   | Pro   |      |
|     |      |       | 290   |       |       |       |       | 295   |       |       |      |       | 300  |       |       |      |
| atg | tgc  | aaa   | ctt   | aat   | ata   | ttg   | aag   | gcc   | ctg   | gga   | att  | gtg   | ccg  | aat   | ttg   | 958  |
| Met | Cys  | Lys   | Leu   | Asn   | Ile   | Leu   | Lys   | Ala   | Leu   | Gly   | Ile  | Val   | Pro  | Asn   | Leu   |      |
|     |      | 305   |       |       |       |       | 310   |       |       |       |      | 315   |      |       |       |      |
| cca | tgt  | act   | gat   | aac   | gta   | gca   | ttc   | gat   | atg   | gaa   | agg  | ctc   | acc  | aga   | acc   | 1006 |
| Pro | Cys  | Thr   | Asp   | Asn   | Val   | Ala   | Phe   | Asp   | Met   | Glu   | Arg  | Leu   | Thr  | Arg   | Thr   |      |
|     | 320  |       |       |       |       | 325   |       |       |       |       | 330  |       |      |       |       |      |
| caa | gct  | gtt   | aac   | cga   | aga   | tca   | gcc   | ctc   | ggc   | gac   | ctc  | gcc   | ggc  | gac   | aac   | 1054 |
| G1n | Ala  | Val   | Asn   | Arg   | Arg   | Ser   | Ala   | Leu   | Gly   | Asp   | Leu  | Ala   | Gly  | Asp   | Asn   |      |
| 335 |      |       |       |       | 340   |       |       |       |       | 345   |      |       |      |       | 350   |      |
| tcc | ctt  | ggc   | ctt   | gag   | cca   | ctt   | cga   | act   | tcg   | ggg   | ato  | tca   | cct  | ctt   | cct   | 1102 |
| Ser | Leu  | Gly   | Leu   | Glu   | Pro   | Leu   | Arg   | Thr   | Ser   | Gly   | Ile  | Ser   | Pro  |       | Pro   |      |
|     |      |       |       | 355   |       |       |       |       | 360   |       |      |       |      | 365   | 5     |      |
| cag | gat  | ggg   | gag   | ctc   | act   | ccg   | aga   | aca   | gga   | gaa   | ato  | aac   | att  | gca   | a gta | 1150 |
| G1n | Asp  | Gly   | Glu   | ı Leu | Thr   | Pro   | Arg   | Thr   | Gly   | Glu   | Ile  | e Ası |      |       | a Val |      |
|     |      |       | 370   | )     |       |       |       | 375   | 5     |       |      |       | 380  | )     |       |      |
|     |      |       |       |       |       |       |       |       |       |       |      |       |      |       | cctc  | 1198 |
| Thr | Lys  | s Glu | ı Trı | o Phe | e Ile | e Ile |       |       | r Phe | e Gly | r Le |       |      | r Ala | a Leu |      |
|     |      | 38    |       |       |       |       | 390   |       |       |       |      | 39    |      |       |       |      |
|     |      |       |       |       |       |       |       | /     |       |       |      |       |      |       | t aat | 1246 |
| Thi | r Le | u Cy  | s Ty  | r Me  | t Il  | e Ile | e Arg | g Ala | a Thi | r Ala | a Se | r Le  | u As | n Al  | a Asn |      |

| 400         | 405               | 5                | 410                |              |
|-------------|-------------------|------------------|--------------------|--------------|
| gag gta gaa | tgg ttt tgaagaa   | igaa aaaacctgct  | ttctgactga ttttgc  | ectt 1300    |
| Glu Val Glu | Trp Phe           | ·                |                    |              |
| 415         |                   |                  |                    |              |
| gaaggaaaaa  | agaacctatt tttgt  | gcatc atttaccaa  | it catgocacac aago | catttat 1360 |
| ttttagtaca  | ttttatttt tcata   | aaatt gctaatgco  | a aagctttgta ttaa  | aaagaaa 1420 |
| taaataataa  | aat               |                  |                    | 1433         |
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| gtatcccccg  | gctacctggg ccgcc  | ccgcg gcggtgcgc  | eg egtgagaggg ageg | gegeggg 60   |
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| tgagcggcgg  | tgtgagcgcg gtggg  | gtgcgg aggggcgtg | gt gtgccggcgc gcgc | egeegtg 180  |
| gggtgcaaac  | cccgagcgtc tacgo  | ctgcc atg agg gg | ge geg aae gee tg  | g gcg 233    |
|             |                   | Met Arg G        | ly Ala Asn Ala Tr  | o Ala        |
|             |                   | 1                | 5                  |              |
| cca ctc tgo | ctg ctg ctg gc    | t gcc gcc acc ca | ag ctc tcg cgg ca  | g cag 281    |
| Pro Leu Cy: | s Leu Leu Leu Ala | a Ala Ala Thr G  | ln Leu Ser Arg Gl  | n Gln        |

| tcc        | cca | gag        | aga | cct | gtt | ttc | aca | tgt | ggt      | ggc | att | ctt | act | gga | gag | 329 |
|------------|-----|------------|-----|-----|-----|-----|-----|-----|----------|-----|-----|-----|-----|-----|-----|-----|
| Ser        | Pro | Glu        | Arg | Pro | Val | Phe | Thr | Cys | Gly      | Gly | Ile | Leu | Thr | Gly | G1u |     |
| <b>2</b> 5 |     | •          |     |     | 30  |     |     |     |          | 35  |     |     |     |     | 40  |     |
| tct        | gga | ttt        | att | ggc | agt | gaa | ggt | ttt | cct      | gga | gtg | tac | cct | cca | aat | 377 |
| Ser        | Gly | Phe        | Ile | Gly | Ser | Glu | Gly | Phe | Pro      | Gly | Val | Tyr | Pro | Pro | Asn |     |
|            |     |            |     | 45  |     |     |     |     | 50       |     |     |     |     | 55  |     |     |
| agc        | aaa | tgt        | act | tgg | aaa | atc | aca | gtt | ссс      | gaa | gga | aaa | gta | gtc | gtt | 425 |
| Ser        | Lys | Cys        | Thr | Trp | Lys | Ile | Thr | Val | Pro      | Glu | Gly | Lys | Val | Val | Val |     |
|            |     |            | 60  |     |     |     |     | 65  |          |     |     |     | 70  |     |     |     |
| ctc        | aat | ttc        | cga | ttc | ata | gac | ctc | gag | agt      | gac | aac | ctg | tgc | cgc | tat | 473 |
| Leu        | Asn | Phe        | Arg | Phe | Ile | Asp | Leu | Glu | Ser      | Asp | Asn | Leu | Cys | Arg | Tyr |     |
|            |     | <b>7</b> 5 |     |     |     |     | 80  |     |          |     |     | 85  |     |     |     |     |
| gac        | ttt | gtg        | gat | gtg | tac | aat | ggc | cat | gcc      | aat | ggc | cag | cgc | att | ggc | 521 |
| Asp        | Phe | Val        | Asp | Val | Tyr | Asn | Gly | His | Ala      | Asn | Gly | Gln | Arg | Ile | Gly |     |
|            | 90  |            |     |     |     | 95  |     |     |          |     | 100 |     |     |     |     |     |
| cgc        | ttc | tgt        | ggc | act | ttc | cgg | cct | gga | gcc      | ctt | gtg | tcc | agt | ggc | aac | 569 |
| Arg        | Phe | Cys        | Gly | Thr | Phe | Arg | Pro | Gly | Ala      | Leu | Val | Ser | Ser | Gly | Asn |     |
| 105        |     |            |     |     | 110 |     |     |     |          | 115 |     |     |     |     | 120 |     |
| aag        | atg | atg        | gtg | cag | atg | att | tct | gat | gcc      | aac | aca | gct | ggc | aat | ggc | 617 |
| Lys        | Met | Met        | Val | Gln | Met | Ile | Ser | Asp | Ala      | Asn | Thr | Ala | Gly | Asn | Gly |     |
|            |     |            |     | 125 |     |     |     |     | 130      |     |     |     |     | 135 |     |     |
| ttc        | atg | gcc        | atg | ttc | tcc | gct | gct | gaa | cca      | aac | gaa | aga | ggg | gat | cag | 665 |
| Phe        | Met | Ala        | Met | Phe | Ser | Ala | Ala | Glu | Pro      | Asn | Glu | Arg | Gly | Asp | Gln |     |
|            |     |            | 140 |     |     |     |     | 145 | ۱۰۰ تشمی |     |     |     | 150 | )   |     |     |
| tat        | tgt | gga        | gga | ctc | ctt | gac | aga | cct | tcc      | ggc | tct | ttt | aaa | acc | ccc | 713 |

| Tyr | Cys | Gly | Gly | Leu | Leu | Asp | Arg | Pro | Ser | Gly | Ser | Phe | Lys | Thr | Pro |      |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|------|
|     |     | 155 |     |     |     |     | 160 |     |     |     |     | 165 |     |     |     |      |
| aac | tgg | cca | gac | cgg | gat | tac | cct | gca | gga | gtc | act | tgt | gtg | tgg | cac | 761  |
| Asn | Trp | Pro | Asp | Arg | Asp | Tyr | Pro | Ala | Gly | Val | Thr | Cys | Val | Trp | His |      |
|     | 170 |     |     |     |     | 175 |     |     |     |     | 180 |     |     |     |     |      |
| att | gta | gcc | cca | aag | aat | cag | ctt | ata | gaa | tta | aag | ttt | gag | aag | ttt | 809  |
| Ile | Val | Ala | Pro | Lys | Asn | Gln | Leu | Ile | Glu | Leu | Lys | Phe | Glu | Lys | Phe |      |
| 185 |     |     |     |     | 190 |     |     |     |     | 195 |     |     |     |     | 200 |      |
| gat | gtg | gag | cga | gat | aac | tac | tgc | cga | tat | gat | tat | gtg | gct | gtg | ttt | 857  |
| Asp | Val | Glu | Arg | Asp | Asn | Tyr | Cys | Arg | Tyr | Asp | Tyr | Val | Ala | Val | Phe |      |
|     |     |     |     | 205 |     |     |     |     | 210 |     |     |     |     | 215 |     |      |
| aat | ggc | ggg | gaa | gtc | aac | gat | gct | aga | aga | att | gga | aag | tat | tgt | ggt | 905  |
| Asn | Gly | Gly | Glu | Val | Asn | Asp | Ala | Arg | Arg | Ile | Gly | Lys | Tyr | Cys | Gly |      |
|     |     |     | 220 |     |     |     |     | 225 |     |     |     |     | 230 |     |     |      |
| gat | agt | cca | cct | gcg | cca | att | gtg | tct | gag | aga | aat | gaa | ctt | ctt | att | 953  |
| Asp | Ser | Pro | Pro | Ala | Pro | Ile | Val | Ser | Glu | Arg | Asn | Glu | Leu | Leu | Ile |      |
|     |     | 235 |     |     |     |     | 240 |     |     |     |     | 245 |     |     |     |      |
| cag | ttt | tta | tca | gac | tta | agt | tta | act | gca | gat | ggg | ttt | att | ggt | cac | 1001 |
| Gln | Phe | Leu | Ser | Asp | Leu | Ser | Leu | Thr | Ala | Asp | Gly | Phe | Ile | Gly | His |      |
|     | 250 |     |     |     |     | 255 |     |     |     |     | 260 |     |     |     |     |      |
| tac | ata | ttc | agg | cca | aaa | aaa | ctg | cct | aca | act | aca | gaa | cag | cct | gtc | 1049 |
| Tyr | Ile | Phe | Arg | Pro | Lys | Lys | Leu | Pro | Thr | Thr | Thr | Glu | Gln | Pro | Val |      |
| 265 |     |     |     |     | 270 |     |     |     |     | 275 |     |     |     |     | 280 |      |
| acc | acc | aca | ttc | cct | gta | acc | acg | ggt | tta | aaa | acc | acc | gtg | gcc | ttg | 1097 |
| Thr | Thr | Thr | Phe | Pro | Val | Thr | Thr | Glv | Leu | Lvs | Thr | Thr | Val | Ala | Len |      |

|     |     |     |     | 285 |     |     |     |      | 290    |      |      |      |      | 295 |     |      |
|-----|-----|-----|-----|-----|-----|-----|-----|------|--------|------|------|------|------|-----|-----|------|
| tgt | caa | caa | aag | tgt | aga | cgg | acg | ggg  | act    | ctg  | gag  | ggc  | aat  | tat | tgt | 1145 |
| Cys | G1n | Gln | Lys | Cys | Arg | Arg | Thr | Gly  | Thr    | Leu  | Glu  | Gly  | Asn  | Tyr | Cys |      |
|     |     |     | 300 |     |     |     |     | 305  |        |      |      |      | 310  |     |     |      |
| tca | agt | gac | ttt | gta | tta | gcc | ggc | act  | gtt    | atc  | aca  | acc  | atc  | act | cgc | 1193 |
| Ser | Ser | Asp | Phe | Val | Leu | Ala | Gly | Thr  | Val    | Ile  | Thr  | Thr  | Ile  | Thr | Arg |      |
|     |     | 315 |     |     |     |     | 320 |      |        |      |      | 325  |      |     |     |      |
| gat | ggg | agt | ttg | cac | gcc | aca | gtc | tcg  | atc    | atc  | aac  | atc  | tac  | aaa | gag | 1241 |
| Asp | G1y | Ser | Leu | His | Ala | Thr | Val | Ser  | Ile    | Ile  | Asn  | Ile  | Tyr  | Lys | Glu |      |
|     | 330 |     |     |     |     | 335 |     |      |        |      | 340  |      |      |     |     |      |
| gga | aat | ttg | gcg | att | cag | cag | gcg | ggc  | aag    | aac  | atg  | agt  | gcc  | agg | ctg | 1289 |
| Gly | Asn | Leu | Ala | Ile | Gln | Gln | Ala | Gly  | Lys    | Asn  | Met  | Ser  | Ala  | Arg | Leu |      |
| 345 |     |     |     |     | 350 |     |     |      |        | 355  |      |      |      |     | 360 |      |
| act | gtc | gtc | tgc | aag | cag | tgc | cct | ctc  | ctc    | aga  | aga  | ggt  | cta  | aat | tac | 1337 |
| Thr | Val | Val | Cys | Lys | Gln | Cys | Pro | Leu  | Leu    | Arg  | Arg  | Gly  | Leu  | Asn | Tyr |      |
|     |     |     |     | 365 |     |     |     |      | 370    |      |      |      |      | 375 |     |      |
| att | att | atg | ggc | caa | gta | ggt | gaa | gat  | ggg    | cga  | ggc  | aaa  | atc  | atg | cca | 1389 |
| Ile | Ile | Met | Gly | Gln | Val | Gly | Glu | Asp  | Gly    | Arg  | Gly  | Lys  | Ile  | Met | Pro |      |
|     |     |     | 380 |     |     |     |     | 385  |        |      |      |      | 390  |     | *   |      |
| aac | agc | ttt | atc | atg | atg | ttc | aag | acc  | aag    | aat  | cag  | aag  | ctc  | ctg | gat | 143  |
| Asn | Ser | Phe | Ile | Met | Met | Phe | Lys | Thr  | Lys    | Asn  | Gln  | Lys  | Leu  | Leu | Asp |      |
|     |     | 395 |     |     |     |     | 400 |      |        |      |      | 405  |      |     |     |      |
| gcc | tta | aaa | aat | aag | caa | tgt | taa | cagt | gaa    | ctgt | gtcc | at t | taag | c   |     | 148  |
| Ala | Leu | Lys | Asn | Lys | Gln | Cys |     |      | - نثسو | -    |      |      |      |     |     |      |
|     | 410 | )   |     |     |     | 415 |     |      |        |      |      |      |      |     |     |      |

| tgtattctgc | cattgccttt | gaaagatcta | tgttctctca | gtagaaaaaa | aaatacttat | 1540 |
|------------|------------|------------|------------|------------|------------|------|
| aaaattacat | attctgaaag | aggattccga | aagatgggac | tggttgactc | ttcacatgat | 1600 |
| ggaggtatga | ggcctccgag | atagctgagg | gaagttcttt | gcctgctgtc | agaggagcag | 1660 |
| ctatctgatt | ggaaacctgc | cgacttagtg | cggtgatagg | aagctaaaag | tgtcaagcgt | 1720 |
| tgacagcttg | gaagcgttta | tttatacatc | tctgtaaaag | gatattttag | aattgagttg | 1780 |
| tgtgaagatg | tcaaaaaaag | attttagaag | tgcaatattt | atagtgttat | ttgtttcacc | 1840 |
| ttcaagcctt | tgccctgagg | tgttacaatc | ttgtcttgcg | ttttctaaat | caatgcttaa | 1900 |
| taaaatattt | ttaaagg    |            |            |            |            | 1917 |

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ggaggagagg cgcggggagc caggcctcgg ggcctcggag caaccacccg agcagacgga 180
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Met Leu Gln

1

acc ttg tat gat tac ttc tgg tgg gaa cgt ctg tgg ctg cct gtg aac 281

Thr Leu Tyr Asp Tyr Phe Trp Trp Glú Arg Leu Trp Leu Pro Val Asn

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|     | 5   |     |       |       |       | 10  |     |       |     |     | 15  |     |       |       |       |     |
|-----|-----|-----|-------|-------|-------|-----|-----|-------|-----|-----|-----|-----|-------|-------|-------|-----|
| ttg | acc | tgg | gcc   | gat   | cta   | gaa | gac | cga   | gat | gga | cgt | gtc | tac   | gcc   | aaa   | 329 |
| Leu | Thr | Trp | Ala   | Asp   | Leu   | Glu | Asp | Arg   | Asp | Gly | Arg | Val | Tyr   | Ala   | Lys   |     |
| 20  |     |     |       |       | 25    |     |     |       |     | 30  |     |     |       |       | 35    |     |
| gcc | tca | gat | ctc   | tat   | atc   | acg | ctg | ccc   | ctg | gcc | ttg | ctc | ttc   | ctc   | atc   | 377 |
| Ala | Ser | Asp | Leu   | Tyr   | Ile   | Thr | Leu | Pro   | Leu | Ala | Leu | Leu | Phe   | Leu   | Ile   |     |
|     |     |     |       | 40    |       |     |     |       | 45  |     |     |     |       | 50    |       |     |
| gtt | cga | tac | ttc   | ttt   | gag   | ctg | tac | gtg   | gct | aca | cca | ctg | gct   | gcc   | ctc   | 425 |
| Val | Arg | Tyr | Phe   | Phe   | Glu   | Leu | Tyr | Val   | Ala | Thr | Pro | Leu | Ala   | Ala   | Leu   |     |
|     |     |     | 55    |       |       |     |     | 60    |     |     |     |     | 65    |       |       |     |
| ttg | aac | ata | aag   | gag   | aaa   | act | cgg | ctg   | cgg | gca | cct | ccc | aac   | gcc   | acc   | 473 |
| Leu | Asn | Ile | Lys   | Glu   | Lys   | Thr | Arg | Leu   | Arg | Ala | Pro | Pro | Asn   | Ala   | Thr   |     |
|     |     | 70  |       |       |       |     | 75  |       |     |     |     | 80  |       |       |       |     |
| ttg | gaa | cat | ttc   | tac   | ctg   | acc | agt | ggc   | aag | cag | ccc | aag | cag   | gtg   | gaa   | 521 |
| Leu | Glu | His | Phe   | Tyr   | Leu   | Thr | Ser | Gly   | Lys | Gln | Pro | Lys | Gln   | Val   | Glu   |     |
|     | 85  |     |       |       |       | 90  |     |       |     |     | 95  |     |       |       |       |     |
| gta | gag | ctt | ttg   | tcc   | cgg   | cag | agc | ggg   | ctc | tct | ggc | cgc | cag   | gta   | gag   | 569 |
| Val | Glu | Leu | Leu   | Ser   | Arg   | Gln | Ser | Gly   | Leu | Ser | Gly | Arg | Gln   | Val   | Glu   |     |
| 100 |     |     |       |       | 105   |     |     |       | ٠   | 110 |     |     |       |       | 115   |     |
| cgt | tgg | ttc | cgt   | cgc   | cgc   | cgc | aac | cag   | gac | cgg | ccc | agt | cto   | cto   | aag   | 617 |
| Arg | Trp | Phe | Arg   | Arg   | Arg   | Arg | Asn | Gln   | Asp | Arg | Pro | Ser | Leu   | ı Let | Lys   |     |
|     |     |     |       | 120   | )     |     |     |       | 125 | •   |     |     |       | 130   | )     |     |
| aag | tto | cga | a gaa | gcc   | ago   | tgg | aga | ttc   | aca | ttt | tac | ctg | g ati | t gco | ttc   | 665 |
| Lys | Phe | Arg | g Glu | ı Ala | s Ser | Trp | Are | g Phe | Ţhr | Phe | Туг | Leu | ı Ile | e Ala | a Phe |     |
|     |     |     | 135   | 5     |       |     |     | 140   | )   |     |     |     | 14    | 5     |       |     |

| att | gcc | ggc | atg | gcc | gtc | att | gtg | gat | aaa | ccc | tgg | ttc | tat | gac | atg | 713  |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|------|
| Ile | Ala | Gly | Met | Ala | Val | Ile | Val | Asp | Lys | Pro | Trp | Phe | Tyr | Asp | Met |      |
|     |     | 150 |     |     |     |     | 155 |     |     |     |     | 160 |     |     |     |      |
| aag | aaa | gtt | tgg | gag | gga | tat | ссс | ata | cag | agc | act | atc | cct | tcc | cag | 761  |
| Lys | Lys | Val | Trp | Glu | Gly | Tyr | Pro | Ile | Gln | Ser | Thr | Ile | Pro | Ser | Gln |      |
|     | 165 |     |     |     |     | 170 |     |     |     |     | 175 |     |     |     |     |      |
| tat | tgg | tac | tac | atg | att | gaa | ctt | tcc | ttc | tac | tgg | tcc | ctg | ctc | ttc | 809  |
| Tyr | Trp | Tyr | Tyr | Met | Ile | Glu | Leu | Ser | Phe | Tyr | Trp | Ser | Leu | Leu | Phe |      |
| 180 |     |     |     |     | 185 |     |     |     |     | 190 |     |     |     |     | 195 |      |
| agc | att | gcc | tct | gat | gtc | aag | cga | aag | gat | ttc | aag | gaa | cag | atc | atc | 857  |
| Ser | Ile | Ala | Ser | Asp | Val | Lys | Arg | Lys | Asp | Phe | Lys | Glu | Gln | Ile | Ile |      |
|     |     |     |     | 200 |     |     |     |     | 205 |     |     |     |     | 210 |     |      |
| cac | cat | gtg | gcc | acc | atc | att | ctc | atc | agc | ttt | tcc | tgg | ttt | gcc | aat | 905  |
| His | His | Val | Ala | Thr | Ile | Ile | Leu | Ile | Ser | Phe | Ser | Trp | Phe | Ala | Asn |      |
|     |     |     | 215 |     |     |     |     | 220 |     |     |     |     | 225 |     |     |      |
| tac | atc | cga | gct | ggg | act | cta | atc | atg | gct | ctg | cat | gac | tet | tcc | gat | 953  |
| Tyr | Ile | Arg | Ala | Gly | Thr | Leu | Ile | Met | Ala | Leu | His | Asp | Ser | Ser | Asp |      |
|     |     | 230 |     |     |     |     | 235 |     |     |     |     | 240 |     |     |     |      |
| tac | ctg | ctg | gag | tca | gcc | aag | atg | ttt | aac | tac | gcg | gga | tgg | aag | aac | 1001 |
| Tyr | Leu | Leu | Glu | Ser | Ala | Lys | Met | Phe | Asn | Tyr | Ala | Gly | Trp | Lys | Asn |      |
|     | 245 |     |     |     |     | 250 |     |     |     |     | 255 |     |     |     |     |      |
| acc | tgc | aac | aac | atc | ttc | atc | gtc | ttc | gcc | att | gtt | ttt | atc | atc | acc | 1049 |
| Thr | Cys | Asn | Asn | Ile | Phe | Ile | Val | Phe | Ala | Ile | Val | Phe | Ile | Ile | Thr |      |
| 260 |     |     |     |     | 265 |     |     |     |     | 270 |     |     |     |     | 275 |      |
| cga | ctg | gtc | atc | ctg | ссс | ttc | tgg | atc | ctg | cat | tgc | acc | ctg | gtg | tac | 1097 |

| Arg Leu Val | Ile Leu   | Pro Phe   | Trp Ile  | Leu His   | Cys Thr   | Leu  | Val               | Tyr    |      |
|-------------|-----------|-----------|----------|-----------|-----------|------|-------------------|--------|------|
| . •         | 280       |           |          | 285       |           |      | 290               |        |      |
| cca ctg gag | ctc-tat   | cct gcc   | ttc ttt  | ggc tat   | tac ttc   | ttc  | aat               | tcc    | 1145 |
| Pro Leu Glu | Leu Tyr   | Pro Ala   | Phe Phe  | Gly Tyr   | Tyr Phe   | Phe  | Asn               | Ser    |      |
|             | 295       |           | 300      |           |           | 305  |                   |        |      |
| atg atg gga | gtt cta   | cag ctg   | ctg cat  | atc ttc   | tgg gcc   | tac  | ctc               | att    | 1193 |
| Met Met Gly | Val Leu   | Gln Leu   | Leu His  | Ile Phe   | Trp Ala   | Tyr  | Leu               | Ile    |      |
| 310         |           |           | 315      |           | 320       | ı    |                   |        |      |
| ttg cgc atg | gcc cac   | aag ttc   | ata act  | gga aag   | ctg gta   | gaa  | gat               | gaa    | 1241 |
| Leu Arg Met | Ala His   | Lys Phe   | Ile Thr  | Gly Lys   | Leu Val   | Glu  | Asp               | Glu    | •    |
| 325         |           | 330       |          |           | 335       |      |                   |        |      |
| cgc agt gac | cgg gaa   | gaa aca   | gag ago  | tca gag   | ggg gag   | gag  | gct               | gca ·  | 1289 |
| Arg Ser Asp | Arg Glu   | Glu Thr   | Glu Ser  | Ser Glu   | Gly Glu   | Glu  | Ala               | Ala    |      |
| 340         |           | 345       |          | 350       | ı         |      |                   | 355    |      |
| gct ggg gga | gga gca   | aag ago   | cgg cc   | cta gcc   | aat ggo   | cac  | ссс               | atc    | 1337 |
| Ala Gly Gly | Gly Ala   | Lys Ser   | Arg Pro  | Leu Ala   | Asn Gly   | His  | Pro               | Ile    |      |
|             | 360       | ·         |          | 365       |           |      | 370               |        |      |
| ctc aat aac | aac cat   | cgt aag   | g aat ga | c tgaacca | itta ttco | agct | gc ct             | tccca  | 1390 |
| Leu Asn Asn | n Asn His | Arg Lys   | s Asn As | р         |           |      |                   |        |      |
|             | 375       |           | 38       | 0         |           |      |                   |        |      |
| gattaatgca  | taaagcca  | ag gaact  | taccct g | ctccctgcg | g ctatag  | ggtc | actt              | taagct | 1450 |
| ctggggaaaa  | aggagaaa  | igt gagag | ggagag t | tctctgcat | t cctccc  | tcct | tgct <sup>-</sup> | tgtcac | 1510 |
| ccagttgcct  | ttaaacca  | aa ttcta  | aaccag c | ctatcccca | a ggtagg  | ggga | cgtt              | ggttat | 1570 |
| attctgttag  | agggggao  | egg tegt: | attttc c | teçetace  | c gccaag  | tcat | cctt              | tctact | 1630 |
| gcttttgagg  |           |           |          | -         | -         |      |                   |        | 1690 |

216

#### 46 /307

| tgagaatttg | gccccagctg | tttgcctttg | actccctgac | ctccagagcc | agggttgtgc | 1750 |
|------------|------------|------------|------------|------------|------------|------|
| cttattgtcc | catctgtggg | cctcattctg | ccaaagctgg | accaaggcta | acctttctaa | 1810 |
| gctccctaac | ttgggccaga | aaccaaagct | gagcttttaa | ctttctccct | ctatgacaca | 1870 |
| aatgaattga | gggtaggagg | agggtgcaca | taacccttac | cctacctctg | ccaaaaagtg | 1930 |
| ggggctgtac | tggggactgc | tcggatgatc | tttcttagtg | ctacttcttt | cagctgtccc | 1990 |
| tgtagcgaca | ggtctaagat | ctgactgcct | cctttctctg | gcctcttccc | ccttccctct | 2050 |
| tctcttcagc | taggctagct | ggtttggagt | agaatggcaa | ctaattctaa | tttttattta | 2110 |
| ttaaatattt | ggggttttgg | ttttaaagcc | agaattacgg | ctagcaccta | gcatttcagc | 2170 |
| agagggacca | ttttagacca | aaatgtactg | ttaatgggtt | ttttttaaa  | attaaaagat | 2230 |
| taaataaaaa | atattaaata | aaacatgg   |            |            |            | 2258 |

<210> 25

<211> 1973

<212> DNA

<213> Homo sapiens

<220>

<221> CDS

<222> (130)...(1887)

⟨400⟩ 25

gagcagacca ggcccggtgg agaattaggt gctgctggga gctcctgcct cccacaggat 60
tccagctgca gggagcctca gggactctgg gccgcacgga gttgggggca ttccccagag 120
agcgtcgcc atg gtc tgc agg gag cag tta tca aag aat cag gtc aag 168
Met Val Cys Arg Glu Gln Leu Ser Lys Asn Gln Val Lys

1 5 10

tgg gtg ttt gcc ggc att acc tgt gtg tct gtg gtg gtc att gcc gca

| Trp | Val | Phe | Ala | Gly | Ile | Thr | Cys | Val | Ser | Val | Val | Val | Ile | Ala | Ala |     |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
|     | 15  |     |     |     |     | 20  |     |     |     |     | 25  |     |     |     |     |     |
| ata | gtc | ctt | gcc | atc | acc | ctg | cgg | cgg | cca | ggc | tgt | gag | ctg | gag | gcc | 264 |
| Ile | Val | Leu | Ala | Ile | Thr | Leu | Arg | Arg | Pro | Gly | Cys | G1u | Leu | Glu | Ala |     |
| 30  |     |     |     |     | 35  |     |     |     |     | 40  |     |     |     |     | 45  |     |
| tgc | agc | cct | gat | gcc | gac | atg | ctg | gac | tac | ctg | ctg | agc | ctg | ggc | cag | 312 |
| Cys | Ser | Pro | Asp | Ala | Asp | Met | Leu | Asp | Tyr | Leu | Leu | Ser | Leu | Gly | Gln |     |
|     |     |     |     | 50  |     |     |     |     | 55  |     |     |     |     | 60  |     |     |
| atc | agc | cgg | cga | gat | gcc | ttg | gag | gtc | acc | tgg | tac | cac | gca | gcc | aac | 360 |
| Ile | Ser | Arg | Arg | Asp | Ala | Leu | Glu | Val | Thr | Trp | Tyr | His | Ala | Ala | Asn |     |
|     |     |     | 65  |     |     |     |     | 70  |     |     |     |     | 75  |     |     |     |
| agc | aag | aaa | gcc | atg | aca | gct | gcc | ctg | aac | agc | aac | atc | aca | gtc | ctg | 408 |
| Ser | Lys | Lys | Ala | Met | Thr | Ala | Ala | Leu | Asn | Ser | Asn | Ile | Thr | Val | Leu |     |
|     |     | 80  |     |     |     |     | 85  |     |     |     |     | 90  |     |     |     |     |
| gag | gct | gac | gtc | aat | gta | gaa | ggg | ctc | ggc | aca | gcc | aat | gag | aca | gga | 456 |
| Glu | Ala | Asp | Val | Asn | Val | Glu | Gly | Leu | Gly | Thr | Ala | Asn | Glu | Thr | Gly |     |
|     | 95  |     |     |     |     | 100 |     |     |     |     | 105 |     |     |     |     | •   |
| gtt | ccc | atc | atg | gca | cac | ccc | ccc | act | atc | tac | agt | gac | aac | aca | ctg | 504 |
| Val | Pro | Ile | Met | Ala | His | Pro | Pro | Thr | Ile | Tyr | Ser | Asp | Asn | Thr | Leu |     |
| 110 |     |     |     |     | 115 |     |     |     |     | 120 |     |     |     |     | 125 |     |
| gag | cag | tgg | ctg | gac | gct | gtg | ctg | ggc | tct | tcc | caa | aag | ggc | atc | aaa | 552 |
| Glu | Gln | Trp | Leu | Asp | Ala | Val | Leu | Gly | Ser | Ser | Gln | Lys | Gly | Ile | Lys |     |
|     |     |     |     | 130 |     |     |     |     | 135 |     |     |     |     | 140 |     |     |
| ctg | gac | ttc | aag | aac | atc | aag | gca | gtg | ggc | ccc | tcc | ctg | gac | ctc | ctg | 600 |
| Leu | Asp | Phe | Lys | Asn | Ile | Lys | Ala | Val | Gly | Pro | Ser | Leu | Asp | Leu | Leu |     |

|     |     |     | 145 |     |     |     |     | 150 |       |     |     |     | 155 |     |     |     |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-------|-----|-----|-----|-----|-----|-----|-----|
| cgg | cag | ctg | aca | gag | gaa | ggc | aaa | gtc | cgg   | cgg | ccc | ata | tgg | atc | aac | 648 |
| Arg | Gln | Leu | Thr | Glu | Glu | Gly | Lys | Val | Arg   | Arg | Pro | Ile | Trp | Ile | Asn |     |
|     |     | 160 |     |     |     |     | 165 |     |       |     |     | 170 |     |     |     |     |
| gct | gac | atc | tta | aag | ggc | ccc | aac | atg | ctc   | atc | tca | act | gag | gtc | aat | 696 |
| Ala | Asp | Ile | Leu | Lys | Gly | Pro | Asn | Met | Leu   | Ile | Ser | Thr | Glu | Val | Asn |     |
|     | 175 |     |     |     |     | 180 |     |     |       |     | 185 |     |     |     |     |     |
| gcc | aca | cag | ttc | ctg | gcc | ctg | gtc | cag | gag   | aag | tat | ccc | aag | gct | acc | 744 |
| Ala | Thr | Gln | Phe | Leu | Ala | Leu | Val | Gln | Glu   | Lys | Tyr | Pro | Lys | Ala | Thr |     |
| 190 |     |     |     |     | 195 |     |     |     |       | 200 |     |     |     |     | 205 |     |
| cta | tct | cca | ggc | tgg | acc | acc | ttc | tac | atg   | tcc | acg | tcc | cca | aac | agg | 792 |
| Leu | Ser | Pro | Gly | Trp | Thr | Thr | Phe | Tyr | Met   | Ser | Thr | Ser | Pro | Asn | Arg |     |
|     |     |     |     | 210 |     |     |     |     | 215   |     |     |     |     | 220 |     |     |
| acg | tac | acc | caa | gcc | atg | gtg | gag | aag | atg   | cac | gag | ctg | gtg | gga | gga | 840 |
| Thr | Tyr | Thr | Gln | Ala | Met | Val | Glu | Lys | Met   | His | Glu | Leu | Val | Gly | Gly |     |
|     |     |     | 225 |     |     |     |     | 230 |       |     |     |     | 235 |     |     |     |
| gtg | ccc | cag | agg | gtc | acc | ttc | cct | gta | cgg   | tct | tcc | atg | gtg | cgg | gct | 888 |
| Val | Pro | Gln | Arg | Val | Thr | Phe | Pro | Val | Arg   | Ser | Ser | Met | Val | Arg | Ala |     |
|     |     | 240 |     |     |     | ٠   | 245 | ,   |       |     |     | 250 |     |     |     |     |
| gcc | tgg | ссс | cac | ttc | agc | tgg | ctg | ctg | agc   | caa | tct | gag | agg | tac | agc | 936 |
| Ala | Trp | Pro | His | Phe | Ser | Trp | Leu | Leu | Ser   | Gln | Ser | Glu | Arg | Tyr | Ser |     |
|     | 255 |     |     |     |     | 260 |     |     |       |     | 265 |     |     |     |     |     |
| ctg | acg | ctg | tgg | cag | gct | gcc | tcg | gac | ссс   | atg | tcg | gtg | gaa | gat | ctg | 984 |
| Leu | Thr | Leu | Trp | Gln | Ala | Ala | Ser | Asp | Pro   | Met | Ser | Val | Glu | Asp | Leu |     |
| 270 |     |     |     |     | 275 |     |     | ,   | تغمين | 287 |     |     |     |     | 205 |     |

| ctc tac gtc cgg gat aac act gct gtc cac caa gtc tac tat ga | ac atc 1 | .032 |
|--|----------|------|
| Leu Tyr Val Arg Asp Asn Thr Ala Val His Gln Val Tyr Tyr As | sp Ile   |      |
| 290 295 30   | 00       |      |
| ttt gag cct ctc ctg tca cag ttc aag cag ctg gcc ttg aat ge | cc aca   | 1080 |
| Phe Glu Pro Leu Leu Ser Gln Phe Lys Gln Leu Ala Leu Asn A  | la Thr   |      |
| 305 310 315  |          |      |
| cgg aaa cca atg tac tac aca gga ggc agc ctg atc cct ctt c  | tc cag   | 1128 |
| Arg Lys Pro Met Tyr Tyr Thr Gly Gly Ser Leu Ile Pro Leu L  | eu Gln   |      |
| 320 325 330  |          |      |
| ctg cct ggg gat gac ggt ctg aat gtg gag tgg ctg gtt cct g  | ac gtc   | 1176 |
| Leu Pro Gly Asp Asp Gly Leu Asn Val Glu Trp Leu Val Pro A  | sp Val   |      |
| 335 340 345  |          |      |
| cag ggc agc ggt aaa aca gca aca atg acc ctc cca gac aca g  | gaa ggc  | 1224 |
| Gln Gly Ser Gly Lys Thr Ala Thr Met Thr Leu Pro Asp Thr G  | Glu Gly  |      |
| 350 355 360  | 365      |      |
| atg atc ctg ctg aac act ggc ctc gag gga act gtg gct gaa    | aac ccc  | 1272 |
| Met Ile Leu Leu Asn Thr Gly Leu Glu Gly Thr Val Ala Glu    | Asn Pro  |      |
| 370 375  | 380      |      |
| gtg ccc att gtt cat act cca agt ggc aac atc ctg acg ctg    | gag tcc  | 1320 |
| Val Pro Ile Val His Thr Pro Ser Gly Asn Ile Leu Thr Leu    | Glu Ser  |      |
| 385 390 395  |          |      |
| tgc ctg cag cag ctg gcc aca cat ccc gga cac tgg ggc atc    | cat ttg  | 1368 |
| Cys Leu Gln Gln Leu Ala Thr His Pro Gly His Trp Gly Ile    | His Leu  |      |
| 400 405 410  |          |      |
| caa ata gcg gag ccc gca gcc ctc cgg cca tcc ctg gcc ttg    | ctg gca  | 1416 |

| Gln | Ile | Ala | Glu | Pro | Ala | Ala | Leu | Arg | Pro       | Ser | Leu | Ala | Leu | Leu | Ala |      |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----------|-----|-----|-----|-----|-----|-----|------|
|     | 415 |     |     |     |     | 420 |     |     |           |     | 425 |     |     |     |     |      |
| cgc | ctc | tcc | agc | ctt | ggc | ctc | ttg | cat | tgg       | cct | gtg | tgg | gtt | ggg | gcc | 1464 |
| Arg | Leu | Ser | Ser | Leu | Gly | Leu | Ļeu | His | Trp       | Pro | Val | Trp | Val | Gly | Ala |      |
| 430 |     |     |     |     | 435 |     |     |     |           | 440 |     |     |     |     | 445 |      |
| aaa | atc | tcc | cac | ggg | agt | ttt | tcg | gtc | ссс       | ggc | cat | gtg | gct | ggc | aga | 1512 |
| Lys | Ile | Ser | His | Gly | Ser | Phe | Ser | Val | Pro       | Gly | His | Val | Ala | Gly | Arg |      |
|     |     |     |     | 450 |     |     |     |     | 455       |     |     |     |     | 460 |     |      |
| gag | ctg | ctt | aca | gct | gtg | gct | gag | gtc | ttc       | ссс | cac | gtg | act | gtg | gca | 1560 |
| Glu | Leu | Leu | Thr | Ala | Val | Ala | Glu | Val | Phe       | Pro | His | Val | Thr | Val | Ala |      |
|     |     |     | 465 |     |     |     |     | 470 |           |     |     |     | 475 |     |     |      |
| cca | ggc | tgg | cct | gag | gag | gtg | ctg | ggc | agt       | ggc | tac | agg | gaa | cag | ctg | 1608 |
| Pro | Gly | Trp | Pro | Glu | Glu | Val | Leu | Gly | Ser       | Gly | Tyr | Arg | Glu | Gln | Leu |      |
|     |     | 480 |     |     |     |     | 485 |     |           |     |     | 490 |     |     |     |      |
| ctc | aca | gat | atg | cta | gag | ttg | tgc | cag | ggg       | ctc | tgg | caa | cct | gtg | tcc | 1656 |
| Leu | Thr | Asp | Met | Leu | Glu | Leu | Cys | Gln | Gly       | Leu | Trp | Gln | Pro | Val | Ser |      |
|     | 495 | •   |     |     |     | 500 |     |     |           |     | 505 |     |     |     |     |      |
| ttc | cag | atg | cag | gcc | atg | ctg | ctg | ggc | cac       | agc | aca | gct | gga | gcc | ata | 1704 |
| Phe | Gln | Met | Gln | Ala | Met | Leu | Leu | Gly | His       | Ser | Thr | Ala | Gly | Ala | Ile |      |
| 510 |     |     |     |     | 515 |     |     |     |           | 520 |     |     |     |     | 525 |      |
| ggc | agg | ctg | ctg | gca | tcc | tcc | ccc | cgg | gcc       | acc | gtc | aca | gtg | gag | cac | 1752 |
| Gly | Arg | Leu | Leu | Ala | Ser | Ser | Pro | Arg | Ala       | Thr | Val | Thr | Val | Glu | His |      |
|     |     |     |     | 530 |     |     |     |     | 535       |     |     |     |     | 540 |     |      |
| aac | cca | gct | ggg | ggc | gac | tat | gcc | tct | gtg<br>بر | agg | aca | gca | ttg | ctg | gca | 1800 |
| Asn | Pro | Ala | Gly | Gly | Asp | Tyr | Ala | Sér | Val       | Arg | Thr | Ala | Leu | Leu | Ala |      |

545 550 555 gct agg gct gtg gac agg acc cga gtc tac tac agg cta ccc cag ggc 1848 Ala Arg Ala Val Asp Arg Thr Arg Val Tyr Tyr Arg Leu Pro Gln Gly 560 565 570 tac cac aag gac ttg ctg gct cat gtt ggt aga aac tgagcaccca ggggtg 1900 Tyr His Lys Asp Leu Leu Ala His Val Gly Arg Asn 575 580 585 gtgggccagc ggacctcagg gcggaggctt cccacgggga ggcaggaaga aataaaggtc 1960 tttggctttc tcc 1973 <210> 26 <211> 1606 <212> DNA <213> Homo sapiens ⟨220⟩ <221> CDS <222> (135)...(1130) <400> 26 60 attgtgcggc gctggtcccc tcagagggtt cctgctgctg ccggtgcctt ggaccctccc cctcgcttct cgttctactg ccccaggagc ccggcgggtc cgggactccc gtccgtgccg 120 gtgcggcgc cggc atg tgg ctg tgg gag gac cag ggc ggc ctc ctg ggc 170 Met Trp Leu Trp Glu Asp Gln Gly Gly Leu Leu Gly 1 5 10 cct ttc tcc ttc ctg ctg cta gtg ctg ctg ctg gtg acg cgg agc ccg 218

Pro Phe Ser Phe Leu Leu Leu Val Leu Leu Val Thr Arg Ser Pro

|     |     | 15  |     |     |     |     | 20  |     |     |     |     | 25  |     |            |     |     |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|------------|-----|-----|
| gtc | aat | gcc | tgc | ctc | ctc | acc | ggc | agc | ctc | ttc | gtt | cta | ctg | cgc        | gtc | 266 |
| Val | Asn | Ala | Cys | Leu | Leu | Thr | Gly | Ser | Leu | Phe | Val | Leu | Leu | Arg        | Val |     |
|     | 30  |     |     |     |     | 35  |     |     |     |     | 40  |     |     |            |     |     |
| ttc | agc | ttt | gag | ccg | gtg | ccc | tct | tgc | agg | gcc | ctg | cag | gtg | ctc        | aag | 314 |
| Phe | Ser | Phe | Glu | Pro | Val | Pro | Ser | Cys | Arg | Ala | Leu | Gln | Val | Leu        | Lys |     |
| 45  |     |     |     |     | 50  |     |     |     |     | 55  |     |     |     |            | 60  |     |
| ссс | cgg | gac | cgc | att | tct | gcc | atc | gcc | cac | cgt | ggc | ggc | agc | cac        | gac | 362 |
| Pro | Arg | Asp | Arg | Ile | Ser | Ala | Ile | Ala | His | Arg | Gly | Gly | Ser | His        | Asp |     |
|     |     |     |     | 65  |     |     |     |     | 70  |     |     |     |     | <b>7</b> 5 |     |     |
| gcg | ccc | gag | aac | acg | ctg | gcg | gcc | att | cgg | cag | gca | gct | aag | aat        | gga | 410 |
| Ala | Pro | Glu | Asn | Thr | Leu | Ala | Ala | Ile | Arg | Gln | Ala | Ala | Lys | Asn        | Gly |     |
|     |     |     | 80  |     |     |     |     | 85  |     |     |     |     | 90  |            |     |     |
| gca | aca | ggc | gtg | gag | ttg | gac | att | gag | ttt | act | tct | gac | ggg | att        | cct | 458 |
| Ala | Thr | Gly | Val | Glu | Leu | Asp | Ile | Glu | Phe | Thr | Ser | Asp | Gly | Ile        | Pro |     |
|     |     | 95  |     |     |     |     | 100 |     |     |     |     | 105 |     |            |     |     |
| gtc | tta | atg | cac | gat | aac | aca | gta | gat | agg | acg | act | gat | ggg | act        | ggg | 506 |
| Val | Leu | Met | His | Asp | Asn | Thr | Val | Asp | Arg | Thr | Thr | Asp | Gly | Thr        | Gly |     |
|     | 110 |     |     |     |     | 115 |     |     |     |     | 120 |     |     |            |     |     |
| cga | ttg | tgt | gat | ttg | aca | ttt | gaa | caa | att | agg | aag | ctg | aat | cct        | gca | 554 |
| Arg | Leu | Cys | Asp | Leu | Thr | Phe | Glu | Gln | Ile | Arg | Lys | Leu | Asn | Pro        | Ala |     |
| 125 |     |     |     |     | 130 |     |     |     |     | 135 |     |     |     |            | 140 |     |
| gca | aac | cac | aga | ctc | agg | aat | gat | ttc | cct | gat | gaa | aag | atc | cct        | acc | 602 |
| Ala | Asn | His | Arg | Leu | Arg | Asn | Asp | Phe | Pro | Asp | Glu | Lys | Ile | Pro        | Thr |     |
|     |     |     |     | 145 |     |     |     | /   | 150 |     |     |     |     | 155        |     |     |

| cta | agg | gaa   | gct   | gtt | gca | gag | tgc | cta | aac     | cat | aac | ctc | aca | atc | ttc   | 650  |
|-----|-----|-------|-------|-----|-----|-----|-----|-----|---------|-----|-----|-----|-----|-----|-------|------|
| Leu | Arg | Glu   | Ala   | Val | Ala | Glu | Cys | Leu | Asn     | His | Asn | Leu | Thr | Ile | Phe   | . •  |
|     |     |       | 160   |     |     |     |     | 165 |         |     |     |     | 170 |     | •     |      |
| ttt | gat | gtc   | aaa   | ggc | cat | gca | cac | aag | gct     | act | gag | gct | cta | aag | aaa   | 698  |
| Phe | Asp | Val   | Lys   | Gly | His | Ala | His | Lys | Ala     | Thr | Glu | Ala | Leu | Lys | Lys   |      |
|     |     | 175   |       |     |     |     | 180 |     |         |     |     | 185 |     |     |       |      |
| atg | tat | atg   | gaa   | ttt | cct | caa | ctg | tat | aat     | aat | agt | gtg | gtc | tgt | tct   | 746  |
| Met | Tyr | Met   | Glu   | Phe | Pro | Gln | Leu | Tyr | Asn     | Asn | Ser | Val | Val | Cys | Ser   |      |
|     | 190 |       |       |     |     | 195 |     |     |         |     | 200 |     |     |     |       |      |
| ttc | ttg | cca   | gaa   | gtt | atc | tac | aag | atg | aga     | caa | aca | gat | cgg | gat | gta   | 794  |
| Phe | Leu | Pro   | Glu   | Val | Ile | Tyr | Lys | Met | Arg     | Gln | Thr | Asp | Arg | Asp | Val   |      |
| 205 |     |       |       |     | 210 |     |     |     |         | 215 |     |     |     |     | 220   |      |
| ata | aca | gca   | tta   | act | cac | aga | cct | tgg | agc     | cta | agc | cat | aca | gga | gat   | 842  |
| Ile | Thr | Ala   | Leu   | Thr | His | Arg | Pro | Trp | Ser     | Leu | Ser | His | Thr | Gly | Asp   |      |
|     |     |       |       | 225 |     |     |     |     | 230     |     |     |     |     | 235 |       |      |
| ggg | aaa | cca   | cgc   | tat | gat | act | ttc | tgg | aaa     | cat | ttt | ata | ttt | gtt | atg   | 890  |
| Gly | Lys | Pro   | Arg   | Tyr | Asp | Thr | Phe | Trp | Lys     | His | Phe | Ile | Phe | Val | Met   |      |
|     |     |       | 240   |     |     |     |     | 245 |         |     |     |     | 250 |     |       |      |
| atg | gac | att   | ttg   | ctc | gat | tgg | agc | atg | cat     | aat | atc | ttg | tgg | tac | ctg   | 938  |
| Met | Asp | Ile   | Leu   | Leu | Asp | Trp | Ser | Met | His     | Asn | Ile | Leu | Trp | Tyr | Leu   |      |
|     |     | 255   | i     |     |     |     | 260 | )   |         |     |     | 265 | •   |     |       |      |
| tgt | gga | att   | tca:  | gct | ttc | ctc | atg | caa | aag     | gat | ttt | gta | tcc | cce | gcc   | 986  |
| Cys | Gly | Ile   | Ser   | Ala | Phe | Leu | Met | Gln | Lys     | Asp | Phe | Val | Ser | Pro | Ala   |      |
|     | 270 | )     |       |     |     | 275 | ;   | _   | ۵ تشمیق |     | 280 | )   |     |     |       |      |
| tac | tte | g aag | g aag | tgg | tca | gct |     | -   |         |     | gtt | gti | gg1 | tgg | g act | 1034 |

| Tyr Leu Lys Lys Trp Ser Ala Lys Gly Ile Gln Val Val Gly Trp Thu | r        |
|---|----------|
| 285 290 295 300   | )        |
| gtt aat acc ttt gat gaa aag agt tac tac gaa tcc cat ctt ggt tcc | c 1082   |
| Val Asn Thr Phe Asp Glu Lys Ser Tyr Tyr Glu Ser His Leu Gly Ser | r        |
| 305 310 315   |          |
| age tat ate act gae age atg gta gaa gae tge gaa eet cae tte     | 1127     |
| Ser Tyr Ile Thr Asp Ser Met Val Glu Asp Cys Glu Pro His Phe     |          |
| 320 325 330   |          |
| tag actttcacgg tgggacgaaa cgggttcaga aactgccagg ggcctcatac      | 1180     |
| agggatatca aaataccctt tgtgctagcc caggccctgg ggaatcaggt gactcaca | aca 1240 |
| aatgcaatag ttggtcactg catttttacc tgaaccaaag ctaaacccgg tgttgcca | acc 1300 |
| atgcaccatg gcatgccaga gttcaacact gttgctcttg aaaatctggg tctgaaaa | aaa 1360 |
| cgcacaagag cccctgccct gccctagctg aggcacacag ggagacccag tgaggata | aag 1420 |
| cacagattga attgtacaat ttgcagatgc agatgtaaat gcatgggaca tgcatga  | taa 1480 |
| ctcagagttg acattttaaa acttgccaca cttatttcaa atatttgtac tcagcta  | tgt 1540 |
| taacatgtac tgtagacatc aaacttgtgg ccatactaat aaaattatta aaaggag  | cac 1600 |
| taaagg  | 1606     |

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|-------|------|-------------|------|------|------|------|------|------|------|------|-------|------|------|------|-------|-----|---|
| ttctt | ccc  | tg c        | ccgc | ccgg | g gc | cctg | aċcg | tgg  | cttc | ttc  | cccg. | gcct | ga t | ctgc | gcagc | 120 |   |
| ccgg  | ggg  | cg c        | ccag | aagg | a gc | aggc | ggcg | cgg  | gggc | gcg  | ctgg  | gcgg | gg g | aggc | gtggc | 180 |   |
| cggag | gctg | cg g        | cggc | aagc | g gg | ctgg | gact | gct  | cggc | cgc  | ctcc  | tgcc | cg g | cgag | cagct | 240 |   |
| caga  | cc a | tg t        | cg c | ct g | aa g | aa t | gg a | cg t | at c | ta g | tg g  | tt c | tt c | tt a | tc    | 288 |   |
|       | M    | et S        | er P | ro G | lu G | lu T | rp T | hr T | yr L | eu V | al V  | al L | eu L | eu I | le    |     |   |
|       |      | 1           |      |      |      | 5    |      |      |      |      | 10    |      |      |      |       |     |   |
| tcc   | atc  | ccc         | atc  | ggc  | ttc  | ctc  | ttt  | aag  | aaa  | gcc  | ggt   | cct  | ggg  | ctg  | aag   | 336 | I |
| Ser : | Ile  | Pro         | Ile  | Gly  | Phe  | Leu  | Phe  | Lys  | Lys  | Ala  | Gly   | Pro  | Gly  | Leu  | Lys   |     |   |
| 15    |      |             |      |      | 20   |      |      |      |      | 25   |       |      |      |      | 30    |     |   |
| aga   | tgg  | gga         | gca  | gcc  | gct  | gtg  | ggc  | ctg  | ggg  | ctc  | acc   | ctg  | ttc  | acc  | tgt   | 384 | ŧ |
| Arg   | Trp  | Gly         | Ala  | Ala  | Ala  | Val  | Gly  | Leu  | Gly  | Leu  | Thr   | Leu  | Phe  | Thr  | Cys   |     |   |
|       |      |             |      | 35   |      |      |      |      | 40   |      |       |      |      | 45   |       |     |   |
| ggc   | ccc  | cac         | act  | ttg  | cat  | tct  | ctg  | gtc  | acc  | atc  | ctc   | ggg  | acc  | tgg  | gcc   | 432 | 2 |
| Gly   | Pro  | His         | Thr  | Leu  | His  | Ser  | Leu  | Val  | Thr  | Ile  | Leu   | Gly  | Thr  | Trp  | Ala   |     |   |
|       |      |             | 50   |      |      |      |      | 55   |      |      |       |      | 60   |      |       |     |   |
| ctc   | att  | cag         | gcc  | cag  | ccc  | tgc  | tcc  | tgc  | cac  | gcc  | ctg   | gct  | ctg  | gcc  | tgg   | 480 | ) |
| Leu   | Ile  | <u>G</u> ln | Ala  | Gln  | Pro  | Cys  | Ser  | Cys  | His  | Ala  | Leu   | Ala  | Leu  | Ala  | Trp   |     |   |
|       |      | 65          |      |      |      |      | 70   |      |      |      |       | 75   |      |      |       |     |   |
| act   | ttc  | tcc         | tat  | ctc  | ctg  | ttc  | ttc  | cga  | gcc  | ctc  | agc   | ctc  | ctg  | ggc  | ctg   | 52  | 8 |
| Thr   | Phe  | Ser         | Tyr  | Leu  | Leu  | Phe  | Phe  | Arg  | Ala  | Leu  | Ser   | Leu  | Leu  | Gly  | Leu   |     |   |
|       | 80   |             |      |      |      | 85   |      |      |      |      | 90    |      |      |      |       |     |   |
| ccc   | act  | ccc         | acg  | ccc  | ttc  | acc  | aat  | gcc  | gtc  | cag  | ctg   | ctg  | ctg  | acg  | ctg   | 57  | 6 |
| Pro   | Thr  | Pro         | Thr  | Pro  | Phe  | Thr  | Asn  | Ala  | Val  | Gln  | Leu   | Leu  | Leu  | Thr  | Leu   |     |   |

| 95  |     |     |     |     | 100 |     |     |     |     | 105 |     |     |     |     | 110 |     |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
| aag | ctg | gtg | agc | ctg | gcc | agt | gaa | gtc | cag | gac | ctg | cat | ctg | gcc | cag | 624 |
| Lys | Leu | Val | Ser | Leu | Ala | Ser | Glu | Val | Gln | Asp | Leu | His | Leu | Ala | Gln |     |
|     |     |     |     | 115 |     |     |     |     | 120 |     |     |     |     | 125 |     |     |
| agg | aag | gaa | atg | gcc | tca | ggc | ttc | agc | aag | ggg | ссс | acc | ctg | ggg | ctg | 672 |
| Arg | Lys | Glu | Met | Ala | Ser | Gly | Phe | Ser | Lys | Gly | Pro | Thr | Leu | Gly | Leu |     |
|     |     |     | 130 |     |     |     |     | 135 |     |     |     |     | 140 |     |     |     |
| ctg | ccc | gac | gtg | ccc | tcc | ctg | atg | gag | aca | ctc | agc | tac | agc | tac | tgc | 720 |
| Leu | Pro | Asp | Val | Pro | Ser | Leu | Met | Glu | Thr | Leu | Ser | Tyr | Ser | Tyr | Cys |     |
|     |     | 145 |     |     |     |     | 150 |     |     |     |     | 155 |     |     |     |     |
| tac | gtg | gga | atc | atg | aca | ggc | ccg | ttc | ttc | cgc | tac | cgc | acc | tac | ctg | 768 |
| Tyr | Val | Gly | Ile | Met | Thr | Gly | Pro | Phe | Phe | Arg | Tyr | Arg | Thr | Tyr | Leu |     |
|     | 160 |     |     |     |     | 165 |     |     |     |     | 170 |     |     |     |     |     |
| gac | tgg | ctg | gag | cag | ccc | ttc | ccc | ggg | gca | gtg | ссс | agc | ctg | cgg | ссс | 816 |
| Asp | Trp | Leu | Glu | Gln | Pro | Phe | Pro | Gly | Ala | Val | Pro | Ser | Leu | Arg | Pro |     |
| 175 |     |     |     |     | 180 |     |     |     |     | 185 |     |     |     |     | 190 |     |
| ctg | ctg | cgc | cgc | gcc | tgg | ccg | gcc | ccg | ctc | ttc | ggc | ctg | ctg | ttc | ctg | 864 |
| Leu | Leu | Arg | Arg | Ala | Trp | Pro | Ala | Pro | Leu | Phe | G1y | Leu | Leu | Phe | Leu |     |
|     |     |     |     | 195 |     |     |     |     | 200 |     |     |     |     | 205 |     |     |
| ctc | tcc | tct | cac | ctc | ttc | ccg | ctg | gag | gcc | gtg | cgc | gag | gac | gcc | ttc | 912 |
| Leu | Ser | Ser | His | Leu | Phe | Pro | Leu | Glu | Ala | Val | Arg | Glu | Asp | Ala | Phe |     |
|     |     |     | 210 |     |     |     |     | 215 |     |     |     |     | 220 |     |     |     |
| tac | gcc | cgc | ccg | ctg | ссс | gcc | cgc | ctc | ttc | tac | atg | atc | ccc | gtc | ttc | 960 |
| Tyr | Ala | Arg | Pro | Leu | Pro | Ala | Arg | Leu | Phe | Tyr | Met | Ile | Pro | Val | Phe |     |
|     |     | 225 |     |     |     |     | 230 | /   | شمو |     |     | 235 |     |     |     |     |

| ttc | gcc  | ttc   | cgc  | atg   | cgc   | ttc   | tac   | gtg   | gcc   | tgg   | att  | gcc   | gcc   | gag  | tgc     | 1008 |
|-----|------|-------|------|-------|-------|-------|-------|-------|-------|-------|------|-------|-------|------|---------|------|
| Phe | Ala  | Phe   | Arg  | Met   | Arg   | Phe   | Tyr   | Val   | Ala   | Trp   | Ile  | Ala   | Ala   | Glu  | Cys     |      |
|     | 240  |       | .•   |       |       | 245   |       |       |       |       | 250  |       |       |      |         |      |
| ggc | tgc  | att   | gcc  | gcc   | ggc   | ttt   | ggg   | gcc   | tac   | ccc   | gtg  | gcc   | gcc   | aaa  | gcc     | 1056 |
| Gly | Cys  | Ile   | Ala  | Ala   | Gly   | Phe   | Gly   | Ala   | Tyr   | Pro   | Val  | Ala   | Ala   | Lys  | Ala     |      |
| 255 |      |       |      |       | 260   |       |       |       |       | 265   |      |       |       |      | 270     |      |
| cgg | gcc  | gga   | ggc  | ggc   | ccc   | acc   | ctc   | caa   | tgc   | cca   | ссс  | ccc   | agc   | agt  | ccg     | 1104 |
| Arg | Ala  | Gly   | Gly  | Gly   | Pro   | Thr   | Leu   | Gln   | Cys   | Pro   | Pro  | Pro   | Ser   | Ser  | Pro     |      |
|     |      |       |      | 275   |       |       |       |       | 280   |       |      |       |       | 285  |         | ٠    |
| gag | aag  | gcg   | gct  | tcc   | ttg   | gag   | tat   | gac   | tat   | gag   | acc  | atc   | cgc   | aac  | atc     | 1152 |
| Glu | Lys  | Ala   | Ala  | Ser   | Leu   | Glu   | Tyr   | Asp   | Tyr   | Glu   | Thr  | Ile   | Arg   | Asn  | Ile     |      |
|     | Ŧ    |       | 290  |       |       |       |       | 295   |       |       |      |       | 300   |      |         |      |
| gac | tgc  | tac   | agc  | aca   | gat   | ttc   | tgc   | gtg   | cgg   | gtg   | cgc  | gat   | ggc   | atg  | cgg     | 1200 |
| Asp | Cys  | Tyr   | Ser  | Thr   | Asp   | Phe   | Cys   | Val   | Arg   | Val   | Arg  | Asp   | Gly   | Met  | Arg     |      |
|     |      | 305   | ;    |       |       |       | 310   |       |       |       |      | 315   |       |      |         |      |
| tac | tgg  | aac   | atg  | acg   | gtg   | cag   | tgg   | tgg   | ctg   | gcg   | cag  | tat   | ato   | tac  | aag     | 1248 |
| Tyr | Trp  | Asr   | Met  | Thr   | Val   | Gln   | Trp   | Trp   | Leu   | Ala   | Glr  | Tyr   | · Ile | Tyr  | Lys     |      |
|     | 320  | )     |      |       |       | 325   |       |       |       |       | 330  | )     |       |      |         |      |
| agc | gca  | a cct | gcc  | cgt   | tco   | tat   | gto   | ctg   | cgc   | ctt   | tag  | gaago | aga   | aact | cagcc   | 1300 |
| Ser | Ala  | a Pro | Ala  | a Arg | g Ser | Tyr   | Val   | Leu   | ı Arg | g Leu | 1    |       |       |      |         |      |
| 335 |      |       |      |       | 340   | )     |       |       |       | 345   | 5    |       |       |      |         |      |
| ggg | tgcg | ggcg  | gcto | cacgo | ct g  | ggaat | ccca  | ig ca | actti | tggga | a gg | ccaa  | agca  | ggt  | ggatcat | 1360 |
| gag | gago | cgcc  | tgga | accat | tgc 1 | tgctg | gagce | gc c1 | tact  | ggca  | c gg | cctc  | cacc  | cgg  | gctacta | 1420 |
| cct | gage | cttc  | ctg  | acca  | tcc ( | cgctg | gtgco | ct g  | gctge | ccga  | g gg | ccgg  | ctgg  | agt  | cagccct | 1480 |
| gcg | ggg  | gcgg  | ctg  | agcc  | cag   | gggg  | ccaga | aa g  | gcct  | ggga  | c tg | ggtg  | cact  | ggt  | tcctgaa | 1540 |
|     |      |       |      |       |       |       |       |       |       |       |      |       |       |      |         |      |

| gatgcgcgcc         | tatgactaca | tgtgcatggg | cttcgtgctg | ctctccttgg | ccgacaccct | 1600 |
|--------------------|------------|------------|------------|------------|------------|------|
| tcggtactgg         | gcctccatct | acttctgtat | ccacttcctg | gccctggcag | ccctggggct | 1660 |
| ggggctggct         | ttaggtgggg | gcagccccag | ccggcggaag | gcagcatccc | agcccaccag | 1720 |
| ccttgccccg         | gagaagctcc | gggaggagta | agctgtcacg | acgctccctc | tgccagctgg | 1780 |
| tcccgggaat         | tctgtgaacc | aggctgctgt | ctcctcccca | gaaagagtcc | ttaccttgga | 1840 |
| gagggtcctg         | gagagaattt | cctcttcccc | agctaaatac | cctgcctgca | actgaagcag | 1900 |
| acccgggggt         | gtcctccctg | ccctctgccc | agaggccacc | tccactccta | caaaatcaaa | 1960 |
| gtattgtcca         | gacaagagtc | actggcccct | gctccagctt | ctgggtatcc | agagagcact | 2020 |
| gcacttcccc         | aaaacggaag | gggccctgg  | gcagtgggtt | ttgggcaaat | tccctttctt | 2080 |
| tgcatccaca         | atgtggggtc | ggagcttggg | ggcaggtcct | gggagtggga | agcctcttcc | 2140 |
| ttgtgtcttt         | cgctccactt | ttagctcatc | gcaccaatat | tgcagacttg | gaaggaagca | 2200 |
| taagcttccc         | atttcacaaa | ggggaaactg | aggtgcgggt | gcgcgggcct | ggggacggcc | 2260 |
| gtcccatggc         | ttccatctga | gccacctcgg | gaccccagca | ctcctggcgc | cctcttctca | 2320 |
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⟨222⟩ (360)...(629)

<400> 28

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| agga | agag | ca a  | cctg | gaaa | c tg | acag  | gaaa  | gga   | tgac     | aag   | ttgg  | gagt | ca c  | aggt | atatg   | 180 |
|------|------|-------|------|------|------|-------|-------|-------|----------|-------|-------|------|-------|------|---------|-----|
| atgg | gcct | cc c  | catg | tgga | t co | ttag  | tgct  | gtg   | gcag     | agc   | cctt  | gtta | att g | tgct | gggat   | 240 |
| tttc | cctc | ca g  | ctcc | cggc | c gg | gaago | tggg  | cto   | acgt     | ggg   | agct  | cagt | tgc c | ctcc | tgcta   | 300 |
| caga | tctg | gtc t | cttc | ctta | c aa | tggg  | gtgc  | tgg:  | cact     | gtg   | ggto  | ctg  | gtg a | egca | cgtg    | 359 |
| atg  | tac  | atg   | caa  | gat  | tat  | tgg   | agg   | acc   | tgg      | ctc   | aag   | ggg  | ctg   | cgc  | ggc     | 407 |
| Met  | Tyr  | Met   | Gln  | Asp  | Tyr  | Trp   | Arg   | Thr   | Trp      | Leu   | Lys   | Gly  | Leu   | Arg  | Gly     |     |
| 1    |      |       |      | 5    |      |       |       |       | 10       |       |       |      |       | 15   |         | •   |
| ttc  | ttc  | ttc   | gtg  | ggc  | gtc  | ctc   | ttc   | tcg   | gcc      | gtc   | tcc   | atc  | gct   | gcc  | ttc     | 455 |
| Phe  | Phe  | Phe   | Val  | Gly  | Val  | Leu   | Phe   | Ser   | Ala      | Val   | Ser   | Ile  | Ala   | Ala  | Phe     |     |
|      |      |       | 20   |      |      |       |       | 25    |          |       |       |      | 30    |      |         |     |
| tgc  | acc  | ttc   | ctc  | gtg  | ctg  | gcc   | atc   | acc   | cgg      | cat   | cag   | agc  | ctc   | aca  | gac     | 503 |
| Cys  | Thr  | Phe   | Leu  | Val  | Leu  | Ala   | Ile   | Thr   | Arg      | His   | Gln   | Ser  | Leu   | Thr  | Asp     |     |
|      |      | 35    |      |      |      |       | 40    |       |          |       |       | 45   |       |      |         |     |
| ccc  | acc  | agc   | tac  | tac  | ctc  | tcc   | agc   | gtc   | tgg      | agc   | ttc   | att  | tcc   | ttc  | aag     | 551 |
| Pro  | Thr  | Ser   | Tyr  | Tyr  | Leu  | Ser   | Ser   | Val   | Trp      | Ser   | Phe   | Ile  | Ser   | Phe  | Lys     |     |
|      | 50   |       |      |      |      | 55    |       |       |          |       | 60    |      |       |      |         |     |
| tgg  | gcc  | ttc   | ctg  | ctc  | agc  | ctc   | tat   | gcc   | cac      | cgc   | tac   | cgg  | gct   | gac  | ttt     | 599 |
| Trp  | Ala  | Phe   | Leu  | Leu  | Ser  | Leu   | Tyr   | Ala   | His      | Arg   | Tyr   | Arg  | , Ala | Asp  | Phe     |     |
| 65   | ,    |       |      |      | 70   | )     |       |       |          | 75    |       |      | ,     | •    | 80      |     |
| gct  | gac  | ato   | agc  | atc  | cto  | ago   | gat   | ttc   | tga      | ccca  | ggg   | ggtg | 5     |      |         | 640 |
| Ala  | Asp  | Ile   | Ser  | Ile  | Leu  | Ser   | Asp   | Phe   | <b>:</b> |       |       |      |       |      |         |     |
|      |      |       |      | 85   | ,    |       |       |       |          |       |       |      |       |      |         |     |
| agg  | tctc | etge  | acco | tggg | gg 8 | ggcct | tage  | ga co | tgga     | actca | gco   | tct  | gaga  | tgtt | gggaga  | 700 |
| ggc  | tact | tccc  | acco | ccte | gt g | gacco | ccaga | na ct | gţg      | gcaga | aaa   | tac  | acag  | cagg | gacgagt | 760 |
| gtg  | gtc1 | tccc  | agga | agct | gt   | cctg  | ccgt  | tc co | ctt      | tcgag | g gaa | aacc | tgag  | tgtg | ggtagag | 820 |

| aggggatect | gccatgttgt | tcctcatcag | cctggccaga | gggcagcttt | agaccttttc | 880  |
|------------|------------|------------|------------|------------|------------|------|
| aaatgaatct | gttttctttt | ctttcttttt | ttttctttt  | tttttttt   | ttgagatgga | 940  |
| gtcttactct | gtcacccagg | ctggagtgca | gtagtgcgat | ctcagctcac | tgcaacctcc | 1000 |
| gcctcccagg | ttcaagcaat | tctcctgcct | tggcctctca | agtagctggg | attacaggca | 1060 |
| tctgccacca | tgcccggcaa | atttttgtgt | ttttagtaga | gacagggttt | tgccatgttg | 1120 |
| gccaggctgg | tctcgaactc | ctgatctcag | gtgattcacc | cgcctcagcc | ttccaaagtg | 1180 |
| ctgggattat | aggtgtgagc | caccgcgccc | ggcctggatc | tgttttctta | gcacgcagtg | 1240 |
| aggaatcttt | gtacttaagg | ccagggcaac | aaagtcaaga | ggtcaaggtg | tagggccatg | 1300 |
| aggcctggac | ctatgctgca | ggcaagggtt | tccatccccg | ctgccctagg | cactctcttc | 1360 |
| ccaaggccag | gttgggcacc | tggggaggtc | agttcagaaa | tatctagcag | agacetetta | 1420 |
| aacccccatc | ccagcacccc | atcctgttgt | tcccagagct | ggtctcccat | gagtgtgcta | 1480 |
| gagccagata | gccgtggccc | cccacccatc | tcactcacac | acacaggcat | ccatacaccc | 1540 |
| cagaagactt | cccaaatgag | gccagactca | gggtcacggg | gaatgtgctt | ctgcccctgt | 1600 |
| aagggctttg | gggaaggggg | caacatagta | gaggctggaa | agagccccca | aacctgtgcc | 1660 |
| catgccctc  | cagccctgcg | tttccattct | gccttctcag | agtgcccttg | ctgcacccag | 1720 |
| accaccggcc | aggagagacc | ttctctccca | ctccagcccc | tctcactgcc | cttcaactag | 1780 |
| agctttcacc | tttttacatt | tcccttctga | aggacacaaa | tctgcttttc | tgcccataca | 1840 |
| ctggcccaag | ggctcaccta | acttgggagg | gaaggggctg | ttggtacaag | gatgattttc | 1900 |
| tgttagactg | ccattttgca | cggtctcccc | cttcccatct | gatgtgtcct | gcccctcagc | 1960 |
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<210> 29

<211> 1606

<212> DNA

<213≻ Homo sapiens

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| <222> (30)(1250)         | ·<br>: ·    | ٠.          |             |         |
| <400> 29                 |             |             |             |         |
| acctetteeg teggetgaat tg | cggccgt atg | cgc ggc tct | gtg gag tgc | acc 53  |
|                          | Met         | Arg Gly Ser | Val Glu Cys | Thr     |
|                          | 1           |             | 5           |         |
| tgg ggt tgg ggg cac tgt  | gcc ccc agc | ccc ctg ctc | ctt tgg act | cta 101 |
| Trp Gly Trp Gly His Cys  | Ala Pro Ser | Pro Leu Leu | Leu Trp Thr | Leu     |
| 10                       | 15          | 20          |             |         |
| ctt ctg ttt gca gcc cca  | ttt ggc ctg | ctg ggg gag | aag acc cgc | cag 149 |
| Leu Leu Phe Ala Ala Pro  | Phe Gly Leu | Leu Gly Glu | Lys Thr Arg | Gln     |
| 25 30                    |             | 35          |             | 40      |
| gtg tct ctg gag gtc atc  | cct aac tgg | ctg ggc ccc | ctg cag aac | ctg 197 |
| Val Ser Leu Glu Val Ile  | Pro Asn Trp | Leu Gly Pro | Leu Gln Asn | Leu     |
| 45                       |             | 50          | 55          |         |
| ctt cat ata cgg gca gtg  | ggc acc aat | tcc aca ctg | cac tat gtg | tgg 245 |
| Leu His Ile Arg Ala Val  | Gly Thr Asn | Ser Thr Leu | His Tyr Val | Trp     |
| 60                       | 65          | ;           | 70          |         |
| agc agc ctg ggg cct ctg  | gca gtg gta | atg gtg gcc | acc aac acc | ccc 293 |
| Ser Ser Leu Gly Pro Leu  | Ala Val Val | Met Val Ala | Thr Asn Thr | Pro     |
| 75                       | 80          |             | 85          |         |
| cac age ace etg age gte  | aac tgg ago | ctc ctg cta | tcc cct gag | ccc 341 |

His Ser Thr Leu Ser Val Asn Trp Ser Leu Leu Ser Pro Glu Pro

95

90

100

| gat | ggg | ggc | ctg | atg | gtg | ctc | cct | aag | gac  | agc | att | cag | ttt | tct | tct | 389 |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|------|-----|-----|-----|-----|-----|-----|-----|
| Asp | Gly | Gly | Leu | Met | Val | Leu | Pro | Lys | Asp  | Ser | Ile | Gln | Phe | Ser | Ser |     |
| 105 |     |     |     |     | 110 |     |     |     |      | 115 |     |     |     |     | 120 |     |
| gcc | ctt | gtt | ttt | acc | agg | ctg | ctt | gag | ttt  | gac | agc | acc | aac | gtg | tcc | 437 |
| Ala | Leu | Val | Phe | Thr | Arg | Leu | Leu | Glu | Phe  | Asp | Ser | Thr | Asn | Val | Ser |     |
|     |     |     |     | 125 |     |     |     |     | 130  |     |     |     |     | 135 |     |     |
| gat | acg | gca | gca | aag | cct | ttg | gga | aga | cca  | tat | cct | cca | tac | tcc | ttg | 485 |
| Asp | Thr | Ala | Ala | Lys | Pro | Leu | Gly | Arg | Pro  | Tyr | Pro | Pro | Tyr | Ser | Leu |     |
|     |     |     | 140 |     |     |     |     | 145 |      |     |     |     | 150 |     |     |     |
| gcc | gat | ttc | tct | tgg | aac | aac | atc | act | gat  | tca | ttg | gat | cct | gcc | acc | 533 |
| Ala | Asp | Phe | Ser | Trp | Asn | Asn | Ile | Thr | Asp  | Ser | Leu | Asp | Pro | Ala | Thr |     |
|     |     | 155 |     |     |     |     | 160 |     |      |     |     | 165 |     |     |     |     |
| ctg | agt | gcc | aca | ttt | caa | ggc | cac | ссс | atg  | aac | gac | cct | acc | agg | act | 581 |
| Leu | Ser | Ala | Thr | Phe | Gln | Gly | His | Pro | Met  | Asn | Asp | Pro | Thr | Arg | Thr |     |
|     | 170 |     |     |     |     | 175 |     |     |      |     | 180 |     |     |     |     |     |
| ttt | gcc | aat | ggc | agc | ctg | gcc | ttc | agg | gtc  | cag | gcc | ttt | tcc | agg | tcc | 629 |
| Phe | Ala | Asn | Gly | Ser | Leu | Ala | Phe | Arg | Val  | Gln | Ala | Phe | Ser | Arg | Ser |     |
| 185 |     |     |     |     | 190 |     |     |     |      | 195 |     |     |     |     | 200 |     |
| agc | cga | cca | gcc | caa | ccc | cct | cgc | ctc | ctg  | cac | aca | gca | gac | acc | tgt | 677 |
| Ser | Arg | Pro | Ala | Gln | Pro | Pro | Arg | Leu | Leu  | His | Thr | Ala | Asp | Thr | Cys |     |
|     |     |     |     | 205 |     |     |     |     | 210  |     |     |     |     | 215 |     |     |
| cag | cta | gag | gtg | gcc | ctg | att | gga | gcc | tct  | ccc | cgg | gga | aac | cgt | tcc | 725 |
| G1n | Leu | Glu | Val | Ala | Leu | Ile | Gly | Ala | Ser  | Pro | Arg | Gly | Asn | Arg | Ser |     |
|     |     |     | 220 |     |     |     |     | 225 | تئسو |     |     |     | 230 |     |     |     |
| ctg | ttt | ggg | ctg | gag | gta | gcc | aca | ttģ |      | cag | ggc | cct | gac | tgc | ссс | 773 |

| Leu | Phe | Gly   | Leu | Glu | Val   | Ala   | Thr | Leu | Gly   | Gln | Gly   | Pro   | Asp   | Cys         | Pro   |      |
|-----|-----|-------|-----|-----|-------|-------|-----|-----|-------|-----|-------|-------|-------|-------------|-------|------|
|     |     | 235   |     |     |       |       | 240 |     |       |     |       | 245   |       |             |       |      |
| tca | átg | cag   | gag | cag | cac   | tcc   | atc | gac | gat   | gaa | tat   | gca   | ccg   | gcc         | gtc   | 821  |
| Ser | Met | Gln   | Glu | Gln | His   | Ser   | Ile | Asp | Asp   | Glu | Tyr   | Ala   | Pro   | Ala         | Val   |      |
|     | 250 |       |     |     |       | 255   |     |     |       |     | 260   |       |       |             |       |      |
| ttc | cag | ttg   | gac | cag | cta   | ctg   | tgg | ggc | tcc   | ctc | cca   | tca   | ggc   | ttt         | gca   | 869  |
| Phe | Gln | Leu   | Asp | Gln | Leu   | Leu   | Trp | Gly | Ser   | Leu | Pro   | Ser   | Gly   | Phe         | Ala   |      |
| 265 |     |       |     |     | 270   |       |     |     |       | 275 |       |       |       |             | 280   |      |
| cag | tgg | cga   | cca | gtg | gct   | tac   | tcc | cag | aag   | ccg | ggg   | ggc   | cga   | gaa         | tca   | 917  |
| G1n | Trp | Arg   | Pro | Val | Ala   | Tyr   | Ser | Gln | Lys   | Pro | Gly   | Gly   | Arg   | Glu         | Ser   |      |
|     |     |       |     | 285 |       |       |     |     | 290   |     |       |       |       | <b>29</b> 5 |       |      |
| gcc | ctg | ccċ   | tgc | caa | gct   | tcc   | cct | ctt | cat   | cct | gcc   | tta   | gca   | tac         | tct   | 965  |
| Ala | Leu | Pro   | Cys | Gln | Ala   | Ser   | Pro | Leu | His   | Pro | Ala   | Leu   | Ala   | Tyr         | Ser   |      |
|     |     |       | 300 |     |       |       |     | 305 |       |     |       |       | 310   |             |       |      |
| ctt | ccc | cag   | tca | ccc | att   | gtc   | cga | gcc | ttc   | ttt | ggg   | tcc   | cag   | aat         | aac   | 1013 |
| Leu | Pro | Gln   | Ser | Pro | Ile   | Val   | Arg | Ala | Phe   | Phe | Gly   | Ser   | Gln   | Asn         | Asn   |      |
|     |     | 315   |     |     |       |       | 320 |     |       |     |       | 325   |       |             |       |      |
| ttc | tgt | gcc   | ttc | aat | ctg   | acg   | ttc | ggg | gct   | tcc | aca   | ggc   | cct   | ggc         | tat   | 1061 |
| Phe | Cys | Ala   | Phe | Asn | Leu   | Thr   | Phe | Gly | Ala   | Ser | Thr   | G1y   | Pro   | Gly         | Tyr   |      |
|     | 330 | )     |     |     |       | 335   |     |     |       |     | 340   | 1     |       |             |       |      |
| tgg | gac | caa   | cac | tac | ctc   | agc   | tgg | tcg | atg   | ctc | ctg   | ggt   | gtg   | ggo         | ttc   | 1109 |
| Trp | Asp | Gln   | His | Tyr | Leu   | Ser   | Trp | Ser | Met   | Leu | Leu   | G1y   | Val   | Gly         | Phe   |      |
| 345 | ;   |       |     |     | 350   | )     |     |     |       | 355 | 5     |       |       |             | 360   |      |
| cct | cca | a gtg | gac | ggo | ttg   | tcc   | cca | cta | gto   | ctg | ggg   | ato   | ate   | g gca       | gtg   | 1157 |
| Pro | Pro | Val   | Asp | Gly | / Leu | . Ser | Pro | Leu | ı Val | Lei | ı Gly | , Ile | e Met | t Ala       | a Val |      |

365 370 375 gcc ctg ggt gcc cca ggg ctc atg ctg cta ggg ggc ggc ttg gtt ctg 1205 Ala Leu Gly Ala Pro Gly Leu Met Leu Leu Gly Gly Gly Leu Val Leu 380 385 390 ctg ctg cac cac aag aag tac tca gag tac cag tcc ata aat taa 1250 Leu Leu His His Lys Lys Tyr Ser Glu Tyr Gln Ser Ile Asn 395 400 405 ggcccgctct ctggagggaa ggacattact gaacctgtct tgctgtgcct cgaaactctg 1310 gaggttggag catcaagttc cagccggccc cttcactccc ccatcttgct tttctgtgga 1370 acctcagagg ccagcctcga cttcctggag acccccaggt ggggcttcct tcatactttg 1430 ttgggggact ttggaggcgg gcaggggaca gggctattga taaggtcccc ttggtgttgc 1490 cttcttgcat ctccacacat ttcccttgga tgggacttgc aggcctaaat gagaggcatt 1550 ctgactggtt ggctgccctg gaaggcaaga aaatagattt atttttttc acaggg 1606

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<211> 1695

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<213> Homo sapiens

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<221> CDS

⟨222⟩ (53)... (631)

<400> 30

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Met

| act | gcc | gtc   | ggc   | gtg | cag   | gcc   | cag | agg   | cct   | ttg   | ggc   | caa   | agg  | cag   | ccc   | 103 |
|-----|-----|-------|-------|-----|-------|-------|-----|-------|-------|-------|-------|-------|------|-------|-------|-----|
| Thr | Ala | Val   | Gly   | Val | Gln   | Ala   | Gln | Arg   | Pro   | Leu   | Gly   | Gln   | Arg  | Gln   | Pro   |     |
|     |     |       | 5     |     |       |       |     | 10    |       |       |       |       | 15   |       |       |     |
| cgc | cgg | tcc   | ttc   | ttt | gaa   | tcc   | ttc | atc   | cgg   | acc   | ctc   | atc   | atc  | acg   | tgt   | 151 |
| Arg | Arg | Ser   | Phe   | Phe | Glu   | Ser   | Phe | Ile   | Arg   | Thr   | Leu   | Ile   | Ile  | Thr   | Cys   |     |
|     |     | 20    |       |     |       |       | 25  |       |       |       |       | 30    |      |       |       |     |
| gtg | gcc | ctg   | gct   | gtg | gtc   | ctg   | tcc | tcg   | gtc   | tcc   | att   | tgt   | gat  | ggg   | cac   | 199 |
| Val | Ala | Leu   | Ala   | Val | Val   | Leu   | Ser | Ser   | Val   | Ser   | Ile   | Cys   | Asp  | Gly   | His   |     |
|     | 35  |       |       |     |       | 40    |     |       |       |       | 45    |       |      |       |       |     |
| tgg | ctc | ctg   | gct   | gag | gac   | cgc   | ctc | ttc   | ggg   | ctc   | tgg   | cac   | ttc  | tgc   | acc   | 247 |
| Trp | Leu | Leu   | Ala   | Glu | Asp   | Arg   | Leu | Phe   | Gly   | Leu   | Trp   | His   | Phe  | Cys   | Thr   |     |
| 50  |     |       |       |     | 55    |       |     |       |       | 60    |       |       |      |       | 65    |     |
| acc | acc | aac   | cag   | agt | gtg   | ccg   | atc | tgc   | ttc   | aga   | gac   | ctg   | ggc  | cag   | gcc   | 295 |
| Thr | Thr | Asn   | Gln   | Ser | Val   | Pro   | Ile | Cys   | Phe   | Arg   | Asp   | Leu   | Gly  | Gln   | Ala   |     |
|     |     |       |       | 70  |       |       |     |       | 75    |       |       |       |      | 80    |       |     |
| cat | gtg | ccc   | ggg   | ctg | gcc   | gtg   | ggc | atg   | ggc   | ctg   | gta   | cgc   | ago  | gtg   | ggc   | 343 |
| His | Val | Pro   | Gly   | Leu | Ala   | Val   | Gly | Met   | Gly   | Leu   | Val   | Arg   | Ser  | · Val | Gly   |     |
|     |     |       | 85    |     |       |       |     | 90    | 1     |       |       |       | 95   | ;     |       |     |
| gcc | ttg | gco   | gtg   | gtg | gcc   | gcc   | att | ttt   | ggc   | ctg   | g gag | tto   | cto  | ate   | gtg   | 391 |
| Ala | Leu | Ala   | a Val | Val | Ala   | Ala   | Ile | Phe   | Gly   | Leu   | ı Glu | Phe   | Leu  | ı Met | . Val |     |
|     |     | 100   | )     |     |       |       | 105 | 5     |       |       |       | 110   | )    |       |       |     |
| tcc | cag | ttg   | g tgo | gag | gad   | c aaa | cac | tca   | cag   | tgo   | c aag | g tgg | ggto | c atg | g ggt | 439 |
| Ser | Glr | ı Lei | ı Cys | Glu | ı Ası | p Lys | His | s Sei | Glr   | ı Cys | s Ly: | s Tr  | y Va | l Me  | t Gly |     |
|     | 115 | 5     |       |     |       | 120   | )   | /     | ا تشو |       | 129   | 5     |      |       |       |     |
| tco | ate | ct    | c ct  | ct  | g gt  | g tci | tte | c gto | cto   | tc    | c tc  | c gg  | c gg | g ct  | c ctg | 487 |

| Ser Ile Leu Leu Val Ser Phe Val Leu Ser Ser Gly Gly Leu Leu       |      |
|---|------|
| 130 135 140 145   |      |
| ggt ttt gtg atc ctc ctc agg aac caa gtc aca ctc atc ggc ttc acc   | 535  |
| Gly Phe Val Ile Leu Leu Arg Asn Gln Val Thr Leu Ile Gly Phe Thr   |      |
| 150 155 160   |      |
| cta atg ttt tgg tgc gaa ttc act gcc tcc ttc ctc ctc ttc ctg aac   | 583  |
| Leu Met Phe Trp Cys Glu Phe Thr Ala Ser Phe Leu Leu Phe Leu Asn   |      |
| 165 170 175   |      |
| gcc atc agc ggc ctt cac atc aac agc atc acc cat ccc tgg gaa tg    | 630  |
| Ala Ile Ser Gly Leu His Ile Asn Ser Ile Thr His Pro Trp Glu       |      |
| 180 185 190   |      |
| accgtggaaa ttttaggccc cctccaggga catcagattc cacaagaaaa tatggtcaaa | 690  |
| atgggacttt tccagcatgt ggcctctggt ggggctgggt tggacaaggg ccttgaaacg | 750  |
| gctgcctgtt tgccgataac ttgtgggtgg tcagccagaa atggcccggg ggcctctgca | 810  |
| cctggtctgc agggccagag gccaggaggg tgcctcagtg ccaccaactg cacaggctta | 870  |
| gccagatgtt gattttagag gaagaaaaaa acattttaaa actccttctt gaattttctt | 930  |
| ccctggactg gaatacagtt ggaagcacag gggtaactgg tacctgagct agctgcacag | 990  |
| ccaaggatag ttcatgcctg tttcattgac acgtgctggg ataggggctg cagaatccct | 1050 |
| ggggctccca gggttgttaa gaatggatca ttcttccagc taagggtcca atcagtgcct | 1110 |
| attetteeae eageteaaag ggeettegta tgtatgteee tggetteage tttggteatg | 1170 |
| ccaaagaggc agagttcagg attccctcag aatgccctgc acacagtagg tttccaaacc | 1230 |
| atttgactcg gtttgcctcc ctgcccgttg tttaaacctt acaaaccctg gataacccca | 1290 |
| tcttctagca gctggctgtc ccctctggga gctctgccta tcagaaccct accttaaggt | 1350 |
| gggtttcctt ccgagaagag ttcttgagca agctctccca ggagggccca cctgactgct | 1410 |
| aatacacage cetececaag geeegtgtgt geatgtgtet gtettttgtg agggttagae | 1470 |

| agcci          | tcagg | g ca | accat | tttt | t aa | tccca | agaa | cac | attt   | caa | agag | cacgi | ta t | ctag  | accte | 3 | 1530 |
|----------------|-------|------|-------|------|------|-------|------|-----|--------|-----|------|-------|------|-------|-------|---|------|
| ctgga          | actct | g ca | agggg | ggtg | a gg | gggaa | acag | cga | gagc   | ttg | ggta | atga  | tt a | acac  | ccate | 3 | 1590 |
| ctgg           | ggate | gc a | tgga  | ggtg | a ag | gggg  | ccag | gaa | ccag   | tgg | agat | ttcc: | at c | cttg  | ccago | 2 | 1650 |
| acgt           | ctgta | ac t | tctg  | ttca | t ta | aagt  | gctc | cct | ttct   | agt | cctt | t     |      |       |       |   | 1695 |
|                |       |      |       |      |      |       |      |     |        |     |      |       |      |       |       |   |      |
| <210           | > 31  |      |       |      |      |       |      |     |        |     |      |       |      |       |       |   |      |
| <b>&lt;211</b> | > 37  | 7    |       |      |      |       |      |     |        |     |      |       |      |       |       |   |      |
| <212           | > PR  | T    |       |      |      |       |      |     |        |     |      |       |      |       |       |   |      |
| <213           | > Ho  | mo s | apie  | ns   |      |       |      |     |        |     |      |       |      |       |       |   |      |
| <400           | > 31  |      |       |      |      |       |      |     |        |     |      |       |      |       |       |   |      |
| Met            | Asp   | Ser  | Ala   | Leu  | Ser  | Asp   | Pro  | His | Asn    | Gly | Ser  | Ala   | Glu  | Ala   | Gly   |   |      |
| 1              |       |      |       | 5    |      |       |      |     | 10     |     |      |       |      | 15    |       |   |      |
| Gly            | Pro   | Thr  | Asn   | Ser  | Thr  | Thr   | Arg  | Pro | Pro    | Ser | Thr  | Pro   | Glu  | Gly   | Ile   |   |      |
|                |       |      | 20    |      |      |       |      | 25  |        |     |      |       | 30   |       |       |   |      |
| Ala            | Leu   | Ala  | Tyr   | Gly  | Ser  | Leu   | Leu  | Leu | Met    | Ala | Leu  | Leu   | Pro  | Ile   | Phe   |   |      |
|                |       | 35   |       |      |      |       | 40   |     |        |     |      | 45    |      |       |       |   |      |
| Phe            | Gly   | Ala  | Leu   | Arg  | Ser  | Val   | Arg  | Cys | Ala    | Arg | Gly  | Lys   | Asn  | Ala   | Ser   |   |      |
|                | 50    |      |       |      |      | 55    |      |     |        |     | 60   |       |      |       |       |   |      |
| Asp            | Met   | Pro  | Glu   | Thr  | Ile  | Thr   | Ser  | Arg | Asp    | Ala | Ala  | Arg   | Phe  | Pro   | Ile   |   |      |
| 65             |       |      |       |      | 70   |       |      |     |        | 75  | •    |       |      |       | 80    |   |      |
| Ile            | Ala   | Ser  | Cys   | Thr  | Leu  | Leu   | Gly  | Leu | Tyr    | Leu | Phe  | Phe   | Lys  | Ile   | Phe   |   |      |
|                |       |      |       | 85   |      |       |      |     | 90     |     |      |       |      | 95    | •     |   |      |
| Ser            | Gln   | Glu  | Tyr   | Ile  | Asn  | Leu   | Leu  | Leu | Ser    | Met | Tyr  | Phe   | Phe  | e Val | Leu   |   |      |
|                |       |      | 100   | +    |      |       |      | 105 | - نثرو |     |      |       | 110  | )     |       |   |      |

Gly Ile Leu Ala Leu Ser His Thr Ile Ser Pro Phe Met Asn Lys Phe

|     |     | 115 |     |     |     |     | 120 |      |       |     |     | 125 |     |     |     |
|-----|-----|-----|-----|-----|-----|-----|-----|------|-------|-----|-----|-----|-----|-----|-----|
| Phe | Pro | Ala | Ser | Phe | Pro | Asn | Arg | Gl'n | Tyr   | Gln | Leu | Leu | Phe | Thr | Gln |
|     | 130 |     |     |     |     | 135 |     |      |       |     | 140 |     |     |     |     |
| Gly | Ser | G1y | Glu | Asn | Lys | Glu | Glu | Ile  | Ile   | Asn | Tyr | Glu | Phe | Asp | Thr |
| 145 |     |     |     |     | 150 |     |     |      |       | 155 |     |     |     |     | 160 |
| Lys | Asp | Leu | Val | Cys | Leu | Gly | Leu | Ser  | Ser   | Ile | Val | Gly | Val | Trp | Tyr |
|     |     |     |     | 165 |     |     |     |      | 170   |     |     |     |     | 175 |     |
| Leu | Leu | Arg | Lys | His | Trp | Ile | Ala | Asn  | Asn   | Leu | Phe | Gly | Leu | Ala | Phe |
|     |     |     | 180 |     |     |     |     | 185  |       |     |     |     | 190 |     |     |
| Ser | Leu | Asn | Gly | Val | Glu | Leu | Leu | His  | Leu   | Asn | Asn | Val | Ser | Thr | Gly |
|     |     | 195 |     |     |     |     | 200 |      |       |     |     | 205 |     |     |     |
| Cys | Ile | Leu | Leu | Gly | Gly | Leu | Phe | Ile  | Tyr   | Asp | Val | Phe | Trp | Val | Phe |
|     | 210 |     |     |     |     | 215 |     |      |       |     | 220 |     |     |     |     |
| Gly | Thr | Asn | Val | Met | Val | Thr | Val | Ala  | Lys   | Ser | Phe | Glu | Ala | Pro | Ile |
| 225 |     |     |     |     | 230 |     |     |      |       | 235 |     |     |     |     | 240 |
| Lys | Leu | Val | Phe | Pro | Gln | Asp | Leu | Leu  | Glu   | Lys | Gly | Leu | Glu | Ala | Asn |
|     |     |     |     | 245 |     |     |     |      | 250   |     |     |     |     | 255 |     |
| Asn | Phe | Ala | Met | Leu | Gly | Leu | Gly | Asp  | Val   | Val | Ile | Pro | Gly | Ile | Phe |
|     |     |     | 260 |     |     |     |     | 265  | :     |     |     |     | 270 |     |     |
| Ile | Ala | Leu | Leu | Leu | Arg | Phe | Asp | Ile  | Ser   | Leu | Lys | Lys | Asn | Thr | His |
|     |     | 275 |     |     |     |     | 280 |      |       |     |     | 285 |     |     |     |
| Thr | Tyr | Phe | Tyr | Thr | Ser | Phe | Ala | Ala  | Tyr   | Ile | Phe | Gly | Leu | Gly | Leu |
|     | 290 |     |     |     |     | 295 |     |      |       |     | 300 |     |     |     |     |
| Thr | Ile | Phe | Ile | Met | His | Ile | Phe | Lys  | His   | Ala | Gln | Pro | Ala | Leu | Leu |
| 305 |     |     |     |     | 310 |     |     | _    | تعربو | 215 |     |     |     |     | 320 |

Glu

#### 69 / 307

Tyr Leu Val Pro Ala Cys Ile Gly Phe Pro Val Leu Val Ala Leu Ala Lys Gly Glu Val Thr Glu Met Phe Ser Tyr Glu Glu Ser Asn Pro Lys Asp Pro Ala Ala Val Thr Glu Ser Lys Glu Gly Thr Glu Ala Ser Ala Ser Lys Gly Leu Glu Lys Lys Glu Lys <210> 32 <211> 81 <212> PRT <213> Homo sapiens <400> 32 Met Thr Ala His Ser Phe Ala Leu Pro Val Ile Ile Phe Thr Thr Phe Trp Gly Leu Val Gly Ile Ala Gly Pro Trp Phe Val Pro Lys Gly Pro Asn Arg Gly Val Ile Ile Thr Met Leu Val Ala Thr Ala Val Cys Cys Tyr Leu Phe Trp Leu Ile Ala Ile Leu Ala Gln Leu Asn Pro Leu Phe Gly Pro Gln Leu Lys Asn Glu Thr Ile Trp Tyr Val Arg Phe Leu Trp 

| <210 | )> 3: | 3     |      |     |     |     |     |     |      |     |     |            |     |     |     |
|------|-------|-------|------|-----|-----|-----|-----|-----|------|-----|-----|------------|-----|-----|-----|
| <21  | 1> 48 | 37    |      |     |     |     |     |     |      |     |     |            |     |     |     |
| <21  | 2> PI | RT    |      |     |     |     |     |     |      |     |     |            |     |     |     |
| <21: | 3> H  | omo : | sapi | ens |     |     |     |     |      |     |     |            |     |     |     |
| <400 | )> 3: | 3     |      |     |     |     |     |     |      |     |     |            |     |     |     |
| Met  | Gly   | Asp   | Thr  | Gly | Leu | Arg | Lys | Arg | Arg  | Glu | Asp | Glu        | Lys | Ser | Ile |
| 1    |       |       |      | 5   |     |     |     |     | 10   |     |     |            |     | 15  |     |
| Gln  | Ser   | Gln   | Glu  | Pro | Lys | Thr | Thr | Ser | Leu  | Gln | Lys | Glu        | Leu | Gly | Leu |
|      |       |       | 20   |     |     |     |     | 25  |      |     |     |            | 30  |     |     |
| Ile  | Ser   | Gly   | Ile  | Ser | Ile | Ile | Val | Gly | Thr  | Ile | Ile | Gly        | Ser | Gly | Ile |
|      |       | 35    |      |     |     |     | 40  |     |      |     |     | <b>4</b> 5 |     |     |     |
| Phe  | Val   | Ser   | Pro  | Lys | Ser | Val | Leu | Ser | Asn  | Thr | Glu | Ala        | Val | Gly | Pro |
|      | 50    |       |      |     |     | 55  |     |     |      |     | 60  |            |     |     |     |
| Cys  | Leu   | Ile   | Ile  | Trp | Ala | Ala | Cys | Gly | Val  | Leu | Ala | Thr        | Leu | Gly | Ala |
| 65   |       |       |      |     | 70  |     |     |     |      | 75  |     |            |     |     | 80  |
| Leu  | Cys   | Phe   | Ala  | Glu | Leu | Gly | Thr | Met | Ile  | Thr | Lys | Ser        | Gly | Gly | Glu |
|      |       |       | ,    | 85  |     |     |     |     | 90   |     |     |            |     | 95  |     |
| Tyr  | Pro   | Tyr   | Leu  | Met | Glu | Ala | Tyr | Gly | Pro  | Ile | Pro | Ala        | Tyr | Leu | Phe |
|      |       |       | 100  |     | •   |     |     | 105 |      |     |     |            | 110 |     |     |
| Ser  | Trp   | Ala   | Ser  | Leu | Ile | Val | Ile | Lys | Pro  | Thr | Ser | Phe        | Ala | Ile | Ile |
|      |       | 115   |      |     |     |     | 120 |     |      |     |     | 125        |     |     |     |
| Cys  | Leu   | Ser   | Phe  | Ser | Glu | Tyr | Val | Cys | Ala  | Pro | Phe | Tyr        | Val | Gly | Cys |
|      | 130   |       |      |     |     | 135 |     | /   | للمو |     | 140 |            |     |     |     |

| Lys | Pro | Pro | Gln   | Ile | Val | Val | Lys | Cys | Leu   | Ala | Ala | Ala | Ala | Ile | Leu |
|-----|-----|-----|-------|-----|-----|-----|-----|-----|-------|-----|-----|-----|-----|-----|-----|
| 145 |     |     |       |     | 150 |     |     |     |       | 155 |     |     |     |     | 160 |
| Phe | Ile | Ser | Thr   | Val | Asn | Ser | Leu | Ser | Val   | Arg | Leu | Gly | Ser | Tyr | Val |
|     |     |     |       | 165 |     |     |     |     | 170   |     |     |     |     | 175 |     |
| Gln | Asn | Ile | Phe   | Thr | Ala | Ala | Lys | Leu | Val   | Ile | Val | Ala | Ile | Ile | Ile |
|     |     |     | 180   |     |     |     |     | 185 |       |     |     |     | 190 |     |     |
| Ile | Ser | Gly | Leu   | Val | Leu | Leu | Ala | Gln | Gly   | Asn | Thr | Lys | Asn | Phe | Asp |
|     |     | 195 |       |     |     |     | 200 |     |       |     |     | 205 |     |     |     |
| Asn | Ser | Phe | Glu   | Gly | Ala | Gln | Leu | Ser | Val   | Gly | Ala | Ile | Ser | Leu | Ala |
|     | 210 |     |       |     |     | 215 |     |     |       |     | 220 |     |     |     |     |
| Phe | Tyr | Asn | Gly   | Leu | Trp | Ala | Tyr | Asp | Gly   | Trp | Asn | Gln | Leu | Asn | Tyr |
| 225 |     |     |       |     | 230 |     |     |     |       | 235 |     |     |     |     | 240 |
| Ile | Thr | Glu | Glu   | Leu | Arg | Asn | Pro | Tyr | Arg   | Asn | Leu | Pro | Leu | Ala | Ile |
|     |     |     |       | 245 |     |     |     |     | 250   |     |     |     |     | 255 |     |
| Ile | Ile | Gly | Ile   | Pro | Leu | Val | Thr | Ala | Cys   | Tyr | Ile | Leu | Met | Asn | Val |
|     |     |     | 260   |     |     |     |     | 265 |       |     |     |     | 270 |     |     |
| Ser | Tyr | Phe | Thr   | Val | Met | Thr | Ala | Thr | Glu   | Leu | Leu | Gln | Ser | Gln | Ala |
|     |     | 275 |       |     |     |     | 280 |     |       |     |     | 285 |     |     |     |
| Val | Ala | Val | Thr   | Phe | Gly | Asp | Arg | Val | Leu   | Tyr | Pro | Ala | Ser | Trp | Ile |
|     | 290 |     |       |     |     | 295 |     |     |       |     | 300 |     |     |     |     |
| Val | Pro | Leu | Phe   | Val | Ala | Phe | Ser | Thr | Ile   | Gly | Ala | Ala | Asn | Gly | Thr |
| 305 |     |     |       |     | 310 |     |     |     |       | 315 |     |     |     |     | 320 |
| Cys | Phe | Thr | Ala   | Gly | Arg | Leu | Ile | Tyr | Val   | Ala | Gly | Arg | Glu | Gly | His |
|     |     |     |       | 325 |     |     |     |     | 330   | )   |     |     |     | 335 |     |
| Met | Leu | Lvs | . Val | Leu | Ser | Tvr | Ile | Ser | · Val | Are | Arg | Leu | Thr | Pro | Ala |

Pro Ala Ile Ile Phe Tyr Gly Ile Ile Ala Thr Ile Tyr Ile Ile Pro Gly Asp Ile Asn Ser Leu Val Asn Tyr Phe Ser Phe Ala Ala Trp Leu Phe Tyr Gly Leu Thr Ile Leu Gly Leu Ile Val Met Arg Phe Thr Arg Lys Glu Leu Glu Arg Pro Ile Lys Val Pro Val Val Ile Pro Val Leu Met Thr Leu Ile Ser Val Phe Leu Val Leu Ala Pro Ile Ile Ser Lys Pro Thr Trp Glu Tyr Leu Tyr Cys Val Leu Phe Ile Leu Ser Gly Leu Leu Phe Tyr Phe Leu Phe Val His Tyr Lys Phe Gly Trp Ala Gln Lys Ile Ser Lys Pro Ile Thr Met His Leu Gln Met Leu Met Glu Val Val Pro Pro Glu Glu Asp Pro Glu 

⟨210⟩ 34

<211> 375

<212> PRT

<213> Homo sapiens

<400> 34

| Met | Thr        | Pro | Gln   | Pro | Ala   | Gly | Pro | Pro | Asp         | Gly        | Gly | Trp | Gly | Trp | Val |
|-----|------------|-----|-------|-----|-------|-----|-----|-----|-------------|------------|-----|-----|-----|-----|-----|
| .1  |            |     |       | 5   |       |     |     |     | 10          |            |     |     |     | 15  |     |
| Val | Ala        | Ala | Ala   | Ala | Phe   | Ala | Ile | Asn | Gly         | Leu        | Ser | Tyr | Gly | Leu | Leu |
|     |            |     | 20    |     |       |     |     | 25  |             |            |     |     | 30  |     |     |
| Arg | Ser        | Leu | Gly   | Leu | Ala   | Phe | Pro | Asp | Leu         | Ala        | Glu | His | Phe | Asp | Arg |
|     |            | 35  |       |     |       |     | 40  |     |             |            |     | 45  |     |     |     |
| Ser | Ala        | Gln | Asp   | Thr | Ala   | Trp | Ile | Ser | Ala         | Leu        | Ala | Leu | Ala | Val | G1n |
|     | 50         |     |       |     |       | 55  |     |     |             |            | 60  |     |     |     |     |
| Gln | Ala        | Ala | Ser   | Pro | Val   | Gly | Ser | Ala | Leu         | Ser        | Thr | Arg | Trp | Gly | Ala |
| 65  |            |     |       |     | 70    |     |     |     |             | <b>7</b> 5 |     |     |     |     | 80  |
| Arg | Pro        | Val | Val   | Met | Val   | Gly | Gly | Val | Leu         | Ala        | Ser | Leu | Gly | Phe | Val |
|     |            |     |       | 85  |       |     |     |     | 90          |            |     |     |     | 95  |     |
| Phe | Ser        | Ala | Phe   | Ala | Ser   | Gly | Leu | Leu | His         | Leu        | Tyr | Leu | Gly | Leu | Gly |
|     |            |     | 100   |     |       |     |     | 105 |             |            |     |     | 110 |     |     |
| Leu | Leu        | Ala | Gly   | Phe | Gly   | Trp | Ala | Leu | Val         | Phe        | Ala | Pro | Ala | Leu | Gly |
|     |            | 115 |       |     |       |     | 120 |     |             |            |     | 125 |     |     |     |
| Thr | Leu        | Ser | Arg   | Tyr | Phe   | Ser | Arg | Arg | Arg         | Val        | Leu | Ala | Val | Gly | Leu |
|     | 130        |     |       |     |       | 135 |     |     |             |            | 140 |     |     |     |     |
| Ala | Leu        | Thr | Gly   | Asn | Gly   | Ala | Ser | Ser | Leu         | Leu        | Leu | Ala | Pro | Ala | Leu |
| 145 |            |     |       |     | 150   |     |     |     |             | 155        |     |     |     |     | 160 |
| Gln | Leu        | Leu | Leu   | Asp | Thr   | Phe | Gly | Trp | Arg         | Gly        | Ala | Leu | Leu | Leu | Leu |
|     |            |     |       | 165 | •     |     |     |     | 170         |            |     |     |     | 175 |     |
| Gly | Ala        | Ile | Thr   | Leu | His   | Leu | Thr | Pro | Cys         | Gly        | Ala | Leu | Leu | Leu | Pro |
|     |            |     | 180   | )   |       |     |     | 185 | ۱۰۰۰ تشمیق. |            |     |     | 190 | )   |     |
| Leu | <b>Val</b> | Leu | ı Pro | Gly | / Asp | Pro | Pro | Ala | Pro         | Pro        | Arg | Ser | Pro | Leu | Ala |

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| 19         | 5       |         |     | 200 |     |     |     |      | 205 |     |     |     |
|------------|---------|---------|-----|-----|-----|-----|-----|------|-----|-----|-----|-----|
| Ala Leu Gl | y Leu S | Ser Leu | Phe | Thr | Arg | Arg | Ala | Phe  | Ser | Ile | Phe | Ala |
| 210        |         |         | 215 |     |     |     |     | 220  |     |     |     |     |
| Leu Gly Th | r Ala I | Leu Val | Gly | Gly | Gly | Tyr | Phe | Val  | Pro | Tyr | Val | His |
| 225        |         | 230     |     |     |     |     | 235 |      |     |     |     | 240 |
| Leu Ala Pr | o Arg I | Phe Arg | Pro | Gly | Pro | Gly | Gly | Ile  | Arg | Ser | Ser | Ala |
|            | 4       | 245     |     |     |     | 250 |     |      |     |     | 255 |     |
| Gly Gly Gl | y Arg ( | Gly Cys | Asp | Gly | Gly | Cys | Gly | Arg  | Pro | Ala | Gly | Leu |
|            | 260     |         |     |     | 265 |     |     |      |     | 270 |     |     |
| Arg Val Al | a Gly   | Arg Pro | Arg | Leu | Gly | Ala | Pro | Pro  | Ala | Ala | Ala | Gly |
| 27         | 5       |         |     | 280 |     |     |     | •    | 285 |     |     |     |
| Arg Ile Ar | g Gly   | Ser Asp | Trp | Ala | Gly | Ala | Val | G1 y | Gly | Gly | Ala | Gly |
| 290        |         |         | 295 |     |     |     |     | 300  |     |     |     |     |
| Ala Arg G  | y Gly   | Arg Arg | Arg | Glu | Leu | Gly | Gly | Ser  | Pro | Ala | Gly | Arg |
| 305        |         | 310     |     |     |     |     | 315 |      |     |     |     | 320 |
| Gly Cys G  | ly Leu  | Trp Ala | Glu | Arg | Gly | Glu | Leu | Arg  | Pro | Ala | Gly | Phe |
|            |         | 325     |     |     |     | 330 |     |      |     |     | 335 |     |
| Arg Cys T  | nr Pro  | Arg Ala | Gly | Gly | Arg | Arg | Arg | Cys  | Gly | Ala | Gly | His |
|            | 340     |         |     |     | 345 |     |     |      |     | 350 | I   |     |
| Arg Ala G  | ly Asp  | Asp Ala | Asp | Glu | Pro | Arg | Gly | Ala  | Pro | Gly | Pro | Ser |
| 3          | 55      |         |     | 360 |     |     |     |      | 365 | ;   |     |     |
| Pro Val A  | rg Leu  | Pro Lys | Gly | •   |     |     |     |      |     |     |     |     |
| 370        |         |         | 375 | 5   |     |     |     |      |     |     |     |     |

| <211 | > 35  | 50    |       |     |     |       |       |     |         |     |     |     |     |      |     |
|------|-------|-------|-------|-----|-----|-------|-------|-----|---------|-----|-----|-----|-----|------|-----|
| <212 | 2> PF | TS    |       |     |     |       |       |     |         |     |     |     |     |      |     |
| <213 | 8> Ho | omo s | sapie | ens |     |       |       |     | ٠       | •   |     |     |     |      |     |
| <400 | )> 38 | 5     |       |     |     |       |       |     |         |     |     |     |     |      |     |
| Met  | Ala   | Thr   | Thr   | Ala | Ala | Pro   | Ala   | Gly | Gly     | Ala | Arg | Asn | Gly | Ala  | Gly |
| 1    |       |       |       | 5   |     |       |       |     | 10      |     |     |     |     | 15   |     |
| Pro  | Glu   | Trp   | Gly   | Gly | Phe | Glu   | Glu   | Asn | Ile     | Gln | Gly | Gly | Gly | Ser  | Ala |
|      |       |       | 20    |     |     |       |       | 25  |         |     |     |     | 30  |      |     |
| Val  | Ile   | Asp   | Met   | Glu | Asn | Met   | Asp   | Asp | Thr     | Ser | Gly | Ser | Ser | Phe  | Glu |
|      |       | 35    |       |     |     |       | 40    |     |         |     |     | 45  |     |      |     |
| Asp  | Met   | Gly   | Glu   | Leu | His | Gln   | Arg   | Leu | Arg     | Glu | Glu | Glu | Val | Asp  | Ala |
|      | 50    |       |       |     |     | 55    |       |     |         |     | 60  |     |     |      |     |
| Asp  | Ala   | Ala   | Asp   | Ala | Ala | Ala   | Ala   | Glu | Glu     | Glu | Asp | Gly | Glu | Phe  | Leu |
| 65   |       |       |       | k   | 70  |       |       |     |         | 75  |     |     |     |      | 80  |
| Gly  | Met   | Lys   | Gly   | Phe | Lys | Gly   | Gln   | Leu | Ser     | Arg | Gln | Val | Ala | Asp  | Gln |
|      |       |       |       | 85  |     |       |       |     | 90      |     |     |     |     | 95   |     |
| Met  | Trp   | Gln   | Ala   | Gly | Lys | Arg   | Gln   | Ala | Ser     | Arg | Ala | Phe | Ser | Leu  | Tyr |
|      |       |       | 100   |     |     |       |       | 105 |         |     |     |     | 110 |      |     |
| Ala  | Asn   | Ile   | Asp   | Ile | Leu | Arg   | Pro   | Tyr | Phe     | Asp | Val | Glu | Pro | Ala  | Gln |
|      |       | 115   |       |     |     |       | 120   |     |         |     |     | 125 |     |      |     |
| Val  | Arg   | Ser   | Arg   | Leu | Leu | Glu   | Ser   | Met | Ile     | Pro | Ile | Lys | Met | Val  | Asn |
|      | 130   |       |       |     |     | 135   |       |     |         |     | 140 |     |     |      |     |
| Phe  | Pro   | Gln   | Lys   | Ile | Ala | Gly   | Glu   | Leu | Tyr     | Gly | Pro | Leu | Met | Leu  | Val |
| 145  |       |       |       |     | 150 |       |       | ,   | ۰۰ تشمی | 155 |     |     |     |      | 160 |
| Phe  | Thr   | Len   | Val   | Ala | Πla | I 611 | انم آ | Hic | C1 v    | Mat | Ive | Thr | Sam | 4.00 | The |

|     |     |     |     | 165 |     |     |     |     | 170 |     |     |     |     | 175 |     |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
| Ile | Ile | Arg | Glu | Gly | Thr | Leu | Met | Gly | Thr | Ala | Ile | Gly | Thr | Cys | Phe |
|     |     |     | 180 |     |     |     |     | 185 |     |     |     |     | 190 |     |     |
| Gly | Tyr | Trp | Leu | Gly | Val | Ser | Ser | Phe | Ile | Tyr | Phe | Leu | Ala | Tyr | Leu |
|     |     | 195 |     |     |     |     | 200 |     |     |     |     | 205 |     |     |     |
| Cys | Asn | Ala | Gln | Ile | Thr | Met | Leu | Gln | Met | Leu | Ala | Leu | Leu | Gly | Tyr |
|     | 210 |     |     |     |     | 215 |     |     |     |     | 220 |     |     |     |     |
| Gly | Leu | Phe | Gly | His | Cys | Ile | Val | Leu | Phe | Ile | Thr | Tyr | Asn | Ile | His |
| 225 |     |     |     |     | 230 |     |     |     |     | 235 |     |     |     |     | 240 |
| Leu | His | Ala | Leu | Phe | Tyr | Leu | Phe | Trp | Leu | Leu | Val | Gly | Gly | Leu | Ser |
|     |     |     |     | 245 |     |     |     |     | 250 |     |     |     |     | 255 |     |
| Thr | Leu | Arg | Met | Val | Ala | Val | Leu | Val | Ser | Arg | Thr | Val | Gly | Pro | Thr |
|     |     |     | 260 |     |     |     |     | 265 |     |     |     |     | 270 |     |     |
| Gln | Arg | Leu | Leu | Leu | Cys | Gly | Thr | Leu | Ala | Ala | Leu | His | Met | Leu | Phe |
|     |     | 275 |     |     |     |     | 280 |     |     |     |     | 285 |     |     |     |
| Leu | Leu | Tyr | Leu | His | Phe | Ala | Tyr | His | Lys | Val | Val | Glu | Gly | Ile | Leu |
|     | 290 |     |     |     |     | 295 |     |     |     |     | 300 |     |     |     |     |
| Asp | Thr | Leu | Glu | Gly | Pro | Asn | Ile | Pro | Pro | Ile | Gln | Arg | Val | Pro | Arg |
| 305 |     |     |     |     | 310 |     |     |     |     | 315 |     |     |     |     | 320 |
| Asp | Ile | Pro | Ala | Met | Leu | Pro | Ala | Ala | Arg | Leu | Pro | Thr | Thr | Val | Leu |
|     |     |     |     | 325 |     |     |     |     | 330 |     |     |     |     | 335 |     |
| Asn | Ala | Thr | Ala | Lys | Ala | Val | Ala | Val | Thr | Leu | Gln | Ser | His |     |     |
|     |     |     | 340 |     |     |     |     | 345 |     |     |     |     | 350 | ı   |     |

| (21)  | l> 66 | 57    |      |     |     |     |     |      |         |     |     |     |     |     |           |
|-------|-------|-------|------|-----|-----|-----|-----|------|---------|-----|-----|-----|-----|-----|-----------|
| <212  | 2> PI | RT.   |      |     | ·   |     |     |      |         |     |     |     |     |     |           |
| <213  | 3> H  | omo : | sapi | ens |     |     |     |      |         |     |     |     |     |     |           |
| <400  | )> 36 | 5     |      |     |     |     |     |      |         |     |     |     |     |     |           |
| Met   | Ser   | Ser   | Gln  | Pro | Ala | Gly | Asn | Gln  | Thr     | Ser | Pro | Gly | Ala | Thr | G1u       |
| 1     |       |       |      | 5   |     |     |     |      | 10      |     |     |     |     | 15  |           |
| Asp   | Tyr   | Ser   | Tyr  | Gly | Ser | Trp | Tyr | Ile  | Asp     | Glu | Pro | Gln | Gly | Gly | Glu       |
|       |       |       | 20   |     |     |     |     | 25   |         |     |     |     | 30  |     |           |
| Glu   | Leu   | Gln   | Pro  | Glu | Gly | Glu | Val | Pro  | Ser     | Cys | His | Thr | Ser | Ile | Pro       |
|       |       | 35    |      |     |     |     | 40  |      |         |     |     | 45  |     |     |           |
| Pro   | Gly   | Leu   | Tyr  | His | Ala | Cys | Leu | Ala  | Ser     | Leu | Ser | Ile | Leu | Val | Leu       |
|       | 50    |       |      |     |     | 55  |     |      |         |     | 60  |     |     |     |           |
| Leu   | Leu   | Leu   | Ala  | Met | Leu | Val | Arg | Arg  | Arg     | Gln | Leu | Trp | Pro | Asp | Cys       |
| 65    |       |       |      |     | 70  |     |     |      |         | 75  |     |     |     |     | 80        |
| Val   | Arg   | Gly   | Arg  | Pro | Gly | Leu | Pro | Ser  | Pro     | Val | Asp | Phe | Leu | Ala | Gly       |
|       |       |       |      | 85  |     |     |     |      | 90      |     |     |     |     | 95  |           |
| Asp   | Arg   | Pro   | Arg  | Ala | Val | Pro | Ala | Ala  | Val     | Phe | Met | Val | Leu | Leu | Ser       |
|       |       |       | 100  |     |     |     |     | 105  |         |     |     |     | 110 |     |           |
| Ser   | Leu   | Cys   | Leu  | Leu | Leu | Pro | Asp | Glu  | Asp     | Ala | Leu | Pro | Phe | Leu | Thr       |
|       |       | 115   |      |     |     |     | 120 |      |         |     |     | 125 |     |     |           |
| Leu   | Ala   | Ser   | Ala  | Pro | Ser | Gln | Asp | Gly  | Lys     | Thr | Glu | Ala | Pro | Arg | Gly       |
|       | 130   |       |      |     |     | 135 |     |      |         |     | 140 |     |     |     |           |
| Ala   | Trp   | Lys   | Ile  | Leu | Gly | Leu | Phe | Tyr  | Tyr     | Ala | Ala | Leu | Tyr | Tyr | Pro       |
| 145   |       |       |      |     | 150 |     |     |      | ۰۰ نشری | 155 |     |     |     |     | 160       |
| וום ו | 412   | 410   | Cvc  | ۸la | Thr | A1. | C1  | u; - | TL      | 43. | 41. | 17: | 7   | 1   | <b>~1</b> |

|     |     |       |     | 165 |     |     |     |     | 170       |     |      |     |       | 175 |     |
|-----|-----|-------|-----|-----|-----|-----|-----|-----|-----------|-----|------|-----|-------|-----|-----|
| Ser | Thr | Leu   | Ser | Trp | Ala | His | Leu | Gly | Val       | Gln | Val  | Trp | Gln   | Arg | Ala |
|     |     |       | 180 |     |     |     |     | 185 |           |     |      |     | 190   |     |     |
| Glu | Cys | Pro   | Gln | Val | Pro | Lys | Ile | Tyr | Lys       | Tyr | Tyr  | Ser | Leu   | Leu | Ala |
|     |     | 195   |     |     |     |     | 200 |     |           |     |      | 205 |       |     |     |
| Ser | Leu | Pro   | Leu | Leu | Leu | Gly | Leu | Gly | Phe       | Leu | Ser  | Leu | Trp   | Tyr | Pro |
|     | 210 |       |     |     |     | 215 |     |     |           |     | 220  |     |       |     |     |
| Val | Gln | Leu   | Val | Arg | Ser | Phe | Ser | Arg | Arg       | Thr | Gly  | Ala | Gly   | Ser | Lys |
| 225 |     |       |     |     | 230 |     |     |     |           | 235 |      |     |       |     | 240 |
| Gly | Leu | Gln   | Ser | Ser | Tyr | Ser | Glu | Glu | Tyr       | Leu | Arg  | Asn | Leu   | Leu | Cys |
|     |     |       |     | 245 |     |     |     |     | 250       |     |      |     |       | 255 |     |
| Arg | Lys | Lys   | Leu | Gly | Ser | Ser | Tyr | His | Thr       | Ser | Lys  | His | Gly   | Phe | Leu |
|     |     |       | 260 |     |     |     |     | 265 |           |     |      |     | 270   |     |     |
| Ser | Trp | Ala   | Arg | Val | Cys | Leu | Arg | His | Cys       | Ile | Tyr  | Thr | Pro   | Gln | Pro |
|     |     | 275   |     |     |     |     | 280 |     |           |     |      | 285 |       |     |     |
| Gly | Phe | His   | Leu | Pro | Leu | Lys | Leu | Val | Leu       | Ser | Ala  | Thr | Leu   | Thr | Gly |
|     | 290 |       |     |     |     | 295 |     |     |           |     | 300  |     |       |     |     |
| Thr | Ala | Ile   | Tyr | Gln | Val | Ala | Leu | Leu | Leu       | Leu | Val  | Gly | Val   | Val | Pro |
| 305 |     |       | . • |     | 310 |     |     |     |           | 315 |      |     |       |     | 320 |
| Thr | Ile | G1n   | Lys | Val | Arg | Ala | Gly | Val | Thr       | Thr | Asp  | Val | Ser   | Tyr | Leu |
|     |     |       |     | 325 | •   |     |     |     | 330       |     |      |     |       | 335 |     |
| Leu | Ala | Gly   | Phe | Gly | Ile | Val | Leu | Ser | Glu       | Asp | Lys  | Glr | Glu   | Val | Val |
|     |     |       | 340 | )   |     |     |     | 345 | ,         |     |      |     | 350   | ı   |     |
| Glu | Lei | ı Val | Lys | His | His | Leu | Trp | Ala | Leu<br>ند | Glu | (Val | Cys | s Tyr | lle | Ser |
|     |     | 359   | 5   |     |     |     | 360 | ) / |           |     |      | 365 | 5     |     |     |

| Ala | Leu | Val | Leu | Ser | Cys | Leu | Leu | Thr | Phe    | Leu  | Val | Leu  | Met              | Arg | Ser |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|--------|------|-----|------|------------------|-----|-----|
|     | 370 |     |     |     |     | 375 |     |     |        |      | 380 |      |                  |     |     |
| Leu | Val | Thr | His | Arg | Thr | Asn | Leu | Arg | Ala    | Leu  | His | Arg  | Gly              | Ala | Ala |
| 385 |     |     |     |     | 390 |     |     |     |        | 395  |     |      |                  |     | 400 |
| Leu | Asp | Leu | Ser | Pro | Leu | His | Arg | Ser | Pro    | His  | Pro | Ser  | Arg              | Gln | Ala |
|     |     |     |     | 405 |     |     |     |     | 410    |      |     |      |                  | 415 |     |
| Ile | Phe | Cys | Trp | Met | Ser | Phe | Ser | Ala | Tyr    | Gln  | Thr | Ala  | Phe              | Ile | Cys |
|     |     |     | 420 |     |     |     |     | 425 |        |      |     |      | 430              |     |     |
| Leu | Gly | Leu | Leu | Val | Gln | Gln | Ile | Ile | Phe    | Phe  | Leu | Gly  | Thr              | Thr | Ala |
|     |     | 435 |     |     |     |     | 440 |     |        |      |     | 445  |                  |     |     |
| Leu | Ala | Phe | Leu | Val | Leu | Met | Pro | Val | Leu    | His  | Gly | Arg  | Asn              | Leu | Leu |
|     | 450 |     |     |     |     | 455 |     |     |        |      | 460 |      |                  |     |     |
| Leu | Phe | Arg | Ser | Leu | Glu | Ser | Ser | Trp | Pro    | Phe  | Trp | Leu  | Thr              | Leu | Ala |
| 465 |     |     |     |     | 470 |     |     |     |        | 475  |     |      |                  |     | 480 |
| Leu | Ala | Val | Ile | Leu | Gln | Asn | Met | Ala | Ala    | His  | Trp | Val  | Phe              | Leu | Glu |
|     |     |     |     | 485 |     |     |     |     | 490    |      |     |      |                  | 495 |     |
| Thr | His | Asp | Gly | His | Pro | Gln | Leu | Thr | Asn    | Arg  | Arg | Val  | Leu              | Tyr | Ala |
|     |     |     | 500 |     |     |     |     | 505 |        |      |     |      | 510              |     |     |
| Ala | Thr | Phe | Leu | Leu | Phe | Pro | Leu | Asn | Val    | Leu  | Val | Gly  | Ala              | Met | Val |
|     |     | 515 |     |     |     |     | 520 |     |        |      |     | 525  |                  |     |     |
| Ala | Thr | Trp | Arg | Val | Leu | Leu | Ser | Ala | Leu    | Tyr  | Asn | Ala  | Ile              | His | Leu |
|     | 530 |     |     |     |     | 535 |     |     |        | ·    | 540 |      |                  |     |     |
| G1y | Gln | Met | Asp | Leu | Ser | Leu | Leu | Pro | Pro    | Arg  | Ala | Ala  | Thr              | Leu | Asp |
| 545 |     |     |     |     | 550 |     |     | ,   | ۰۰ نغر | 555  |     |      |                  |     | 560 |
| Pro | Glv | Tyr | Tyr | Thr | Tvr | Arø | Asn | Phe | Leu    | I.vs | Πe  | Glii | V <sub>a</sub> 1 | Ser | Gln |

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80 /307

570 575 565 Ser His Pro Ala Met Thr Ala Phe Cys Ser Leu Leu Cln Ala Gln 590 580 . 585 Ser Leu Leu Pro Arg Thr Met Ala Ala Pro Gln Asp Ser Leu Arg Pro 600 605 595 Gly Glu Glu Asp Glu Gly Met Gln Leu Leu Gln Thr Lys Asp Ser Met 615 620 610 Ala Lys Gly Ala Arg Pro Gly Ala Ser Arg Gly Arg Ala Arg Trp Gly 630 635 640 625 Leu Ala Tyr Thr Leu Leu His Asn Pro Thr Leu Gln Val Phe Arg Lys 645 650 655 Thr Ala Leu Leu Gly Ala Asn Gly Ala Gln Pro 665 660 <210> 37 <211> 464

<212> PRT

<213> Homo sapiens

<400> 37

Met Ile Val Cys Leu Leu Phe Met Met Ile Leu Leu Ala Lys Glu Val

1 5 10 15

Gln Leu Val Asp Gln Thr Asp Ser Pro Leu Leu Ser Leu Leu Gly Gln

20 25 30

Thr Ser Ser Leu Ser Trp His Leu Val Asp Ile Val Ser Tyr Gln Ser

35 40 / 45

| Val | Leu | Ser | Tyr | Phe | Ser | Ser | His | Tyr | Pro    | Pro | Ser | Ile | Ile | Leu | Ala |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|--------|-----|-----|-----|-----|-----|-----|
|     | 50  |     |     |     |     | 55  |     |     |        |     | 60  |     |     |     |     |
| Lys | Glu | Ser | Tyr | Ala | Glu | Leu | Ile | Met | Lys    | Leu | Leu | Lys | Val | Ser | Ala |
| 65  |     |     |     |     | 70  |     |     |     |        | 75  |     |     |     |     | 80  |
| Gly | Leu | Ser | Ile | Pro | Thr | Asp | Ser | Gln | Lys    | His | Leu | Asp | Ala | Val | Pro |
|     |     |     |     | 85  |     |     |     |     | 90     |     |     |     |     | 95  |     |
| Lys | Cys | Gln | Ala | Phe | Thr | His | Gln | Met | Val    | Gln | Phe | Leu | Ser | Thr | Leu |
|     |     |     | 100 |     |     |     |     | 105 |        |     |     |     | 110 |     |     |
| Glu | Gln | Asn | Gly | Lys | Ile | Thr | Leu | Ala | Val    | Leu | Glu | Gln | Glu | Met | Ser |
|     |     | 115 |     |     |     |     | 120 |     |        |     |     | 125 |     |     |     |
| Lys | Leu | Leu | Asp | Asp | Ile | Ile | Val | Phe | Asn    | Pro | Pro | Asp | Met | Asp | Ser |
|     | 130 |     |     |     |     | 135 |     |     |        |     | 140 |     |     | ٠   |     |
| Gln | Thr | Arg | His | Met | Ala | Leu | Ser | Ser | Leu    | Phe | Met | Glu | Val | Leu | Met |
| 145 |     |     | •   |     | 150 |     |     |     |        | 155 |     |     |     |     | 160 |
| Met | Met | Asn | Asn | Ala | Thr | Ile | Pro | Thr | Ala    | Glu | Phe | Leu | Arg | Gly | Ser |
|     |     |     |     | 165 |     |     |     |     | 170    |     |     |     |     | 175 |     |
| Ile | Arg | Thr | Trp | Ile | G1y | Gln | Lys | Met | His    | Gly | Leu | Val | Val | Leu | Pro |
|     |     |     | 180 |     |     |     |     | 185 |        |     |     |     | 190 |     |     |
| Leu | Leu | Thr | Ala | Ala | Cys | Gln | Ser | Leu | Ala    | Ser | Val | Arg | His | Met | Ala |
|     |     | 195 |     |     |     |     | 200 |     |        |     |     | 205 |     |     |     |
| Glu | Thr | Thr | Glu | Ala | Cys | Ile | Thr | Ala | Tyr    | Phe | Lys | Glu | Ser | Pro | Leu |
|     | 210 |     |     |     |     | 215 |     |     |        |     | 220 |     |     |     |     |
| Asn | Gln | Asn | Ser | G1y | Trp | Gly | Pro | Ile | Leu    | Val | Ser | Leu | Gln | Val | Pro |
| 225 |     |     |     |     | 230 |     |     |     | - تشرق | 235 |     |     |     |     | 240 |
| Glu | Leu | Thr | Met | G1n | Glu | Phe | Lou | Gln | Cla    | Cva | Lou | Thu | 1   | C1  | C   |

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|     |       |       |       | 245   |       |       |       |       | 250  |     |       |     |       | 255 |     |
|-----|-------|-------|-------|-------|-------|-------|-------|-------|------|-----|-------|-----|-------|-----|-----|
| Tyr | Leu   | Thr   | Leų   | Tyr   | Val   | Tyr   | Leu   | Leu   | Gln  | Cys | Leu   | Asn | Ser   | Glu | Gln |
|     |       |       | 260   |       |       |       |       | 265   |      |     |       |     | 270   |     |     |
| Thr | Leu   | Arg   | Asn   | Glu   | Met   | Lys   | Val   | Leu   | Leu  | Ile | Leu   | Ser | Lys   | Trp | Leu |
|     |       | 275   |       |       |       |       | 280   |       |      |     |       | 285 |       |     |     |
| Glu | Gln   | Val   | Tyr   | Pro   | Ser   | Ser   | Val   | Glu   | Glu  | Glu | Ala   | Lys | Leu   | Phe | Leu |
|     | 290   |       |       |       |       | 295   |       |       |      |     | 300   |     |       |     |     |
| Trp | Trp   | His   | Gln   | Val   | Leu   | Gln   | Leu   | Ser   | Leu  | Ile | Gln   | Thr | Glu   | Gln | Asn |
| 305 |       |       |       |       | 310   |       |       |       |      | 315 |       |     |       |     | 320 |
| Asp | Ser   | Val   | Leu   | Thr   | Glu   | Ser   | Val   | Ile   | Arg  | Ile | Leu   | Leu | Leu   | Val | Gln |
|     |       |       |       | 325   |       |       |       |       | 330  |     |       |     |       | 335 |     |
| Ser | Arg   | Gln   | Asn   | Leu   | Val   | Ala   | Glu   | Glu   | Arg  | Leu | Ser   | Ser | Gly   | Ile | Leu |
|     |       |       | 340   |       |       |       |       | 345   |      |     |       |     | 350   |     |     |
| Gly | Ala   | Ile   | Gly   | Phe   | Gly   | Arg   | Lys   | Ser   | Pro  | Leu | Ser   | Asn | Arg   | Phe | Arg |
|     |       | 355   |       |       |       |       | 360   |       |      |     |       | 365 |       |     |     |
| Val | Val   | Ala   | Arg   | Ser   | Met   | Ala   | Ala   | Phe   | Leu  | Ser | Val   | Gln | Val   | Pro | Met |
|     | 370   |       |       |       |       | 375   |       |       |      |     | 380   |     |       |     |     |
| Glu | Asp   | Gln   | Ile   | Arg   | Leu   | Arg   | Pro   | Gly   | Ser  | Glu | Leu   | His | Leu   | Thr | Pro |
| 385 |       |       |       |       | 390   | ı     | ,     |       |      | 395 |       |     |       |     | 400 |
| Lys | Ala   | Glr   | Glr   | Ala   | Leu   | Asn   | Ala   | Leu   | Glu  | Ser | Met   | Ala | Ser   | Ser | Lys |
|     |       |       |       | 405   | 5     |       |       |       | 410  | )   |       |     |       | 415 |     |
| Glr | Tyr   | · Val | Glu   | ı Tyr | Gln   | Asp   | Gln   | lle   | Leu  | Glr | Ala   | Thr | - Gln | Phe | Ile |
|     |       |       | 420   | )     |       |       |       | 425   | 5    |     |       |     | 430   | )   |     |
| Arg | g His | s Pro | o Gly | y His | s Cys | s Leu | ı Glr | n Asp | Gly  | Lys | s Ser | Phe | e Leu | Ala | Leu |
|     |       | 43    | 5     |       |       |       | 440   | ) /   | تثمن |     |       | 449 | 5     |     |     |

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Leu Val Asn Cys Leu Tyr Pro Glu Val His Tyr Leu Asp His Ile Arg <210> 38 <211> 470 <212> PRT <213> Homo sapiens <400> 38 Met Ser Arg Leu Gly Ala Leu Gly Gly Ala Arg Ala Gly Leu Gly Leu Leu Leu Gly Thr Ala Ala Gly Leu Gly Phe Leu Cys Leu Leu Tyr Ser Gln Arg Trp Lys Arg Thr Gln Arg His Gly Arg Ser Gln Ser Leu Pro Asn Ser Leu Asp Tyr Thr Gln Thr Ser Asp Pro Gly Arg His Val Met Leu Leu Arg Ala Val Pro Gly Gly Ala Gly Asp Ala Ser Val Leu Pro Ser Leu Pro Arg Glu Gly Gln Glu Lys Val Leu Asp Arg Leu Asp Phe Val Leu Thr Ser Leu Val Ala Leu Arg Arg Glu Val Glu Leu Arg Ser Ser Leu Arg Gly Leu Ala Gly Glu Ile Val Gly Glu Val Arg Cys

His Met Glu Glu Asn Gln Arg Val Ala Arg Arg Arg Phe Pro Phe

|     | 130 |     |     |     |      | 135 |     |     |           |     | 140 |     |     |     |     |
|-----|-----|-----|-----|-----|------|-----|-----|-----|-----------|-----|-----|-----|-----|-----|-----|
| Val | Arg | Glu | Arg | Ser | Asp  | Ser | Thr | Gly | Ser       | Ser | Ser | Val | Tyr | Phe | Thr |
| 145 |     |     |     |     | 150  |     |     |     |           | 155 |     |     |     |     | 160 |
| Ala | Ser | Ser | Gly | Ala | Thr  | Phe | Thr | Asp | Ala       | Glu | Ser | Glu | Gly | Gly | Tyr |
|     |     |     |     | 165 |      |     |     |     | 170       |     |     |     |     | 175 |     |
| Thr | Thr | Ala | Asn | Ala | Glu  | Ser | Asp | Asn | Glu       | Arg | Asp | Ser | Asp | Lys | Glu |
|     |     |     | 180 |     |      |     |     | 185 |           |     |     |     | 190 |     |     |
| Ser | Glu | Asp | Gly | Glu | Asp  | Glu | Val | Ser | Cys       | Glu | Thr | Val | Lys | Met | Gly |
|     |     | 195 |     |     |      |     | 200 |     |           |     |     | 205 |     |     |     |
| Arg | Lys | Asp | Ser | Leu | Asp  | Leu | Glu | Glu | Glu       | Ala | Ala | Ser | Gly | Ala | Ser |
|     | 210 |     |     |     |      | 215 |     |     |           |     | 220 |     |     |     |     |
| Ser | Ala | Leu | Glu | Ala | G1 y | Gly | Ser | Ser | Gly       | Leu | Glu | Asp | Val | Leu | Pro |
| 225 |     |     |     |     | 230  |     |     |     |           | 235 |     |     |     |     | 240 |
| Leu | Leu | Gln | Gln | Ala | Asp  | Glu | Leu | His | Arg       | Gly | Asp | Glu | Gln | Gly | Lys |
|     |     |     |     | 245 |      |     |     |     | 250       |     |     |     |     | 255 |     |
| Arg | Glu | Gly | Phe | Gln | Leu  | Leu | Leu | Asn | Asn       | Lys | Leu | Val | Tyr | Gly | Ser |
|     |     |     | 260 |     |      |     |     | 265 |           |     |     |     | 270 |     |     |
| Arg | Gln | Asp | Phe | Leu | Trp  | Arg | Leu | Ala | Arg       | Ala | Tyr | Ser | Asp | Met | Cys |
|     |     | 275 |     |     |      |     | 280 |     |           |     |     | 285 |     |     |     |
| Glu | Leu | Thr | Glu | Glu | Val  | Ser | Glu | Lys | Lys       | Ser | Tyr | Ala | Leu | Asp | Gly |
|     | 290 |     |     |     |      | 295 |     |     |           |     | 300 |     |     |     |     |
| Lys | Glu | Glu | Ala | Glu | Ala  | Ala | Leu | Glu | Lys       | Gly | Asp | Glu | Ser | Ala | Asp |
| 305 |     |     |     |     | 310  |     |     |     |           | 315 |     |     |     |     | 320 |
| Cys | His | Leu | Trp | Tyr | Ala  | Val | Leu | Cys | Gly<br>نر | Gln | Leu | Ala | Glu | His | Glu |
|     |     |     |     | 325 |      |     |     | /   | 330       |     |     |     |     | 335 |     |

Ser Ile Gln Arg Arg Ile Gln Ser Gly Phe Ser Phe Lys Glu His Val 340 345 350 Asp Lys Ala Ile Ala Leu Gln Pro Glu Asn Pro Met Ala His Phe Leu 355 360 365 Leu Gly Arg Trp Cys Tyr Gln Val Ser His Leu Ser Trp Leu Glu Lys 370 375 380 Lys Thr Ala Thr Ala Leu Leu Glu Ser Pro Leu Ser Ala Thr Val Glu 385 390 395 400 Asp Ala Leu Gln Ser Phe Leu Lys Ala Glu Glu Leu Gln Pro Gly Phe 405 410 415 Ser Lys Ala Gly Arg Val Tyr Ile Ser Lys Cys Tyr Arg Glu Leu Gly 420 425 430 Lys Asn Ser Glu Ala Arg Trp Trp Met Lys Leu Ala Leu Glu Leu Pro 435 440 445 Asp Val Thr Lys Glu Asp Leu Ala Ile Gln Lys Asp Leu Glu Glu Leu 450 455 460 Glu Val Ile Leu Arg Asp 465 470

⟨210⟩ 39

<211> 243

<212> PRT

<213> Homo sapiens

<400> 39

Met Glu Gln Gly Ser Gly Arg Leu Glu Asp Phe Pro Val Asn Val Phe

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| 1   |     |     |     | 5   |     |     |     |     | 10  |     |     |     |     | 15  |     |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
| Ser | Val | Thr | Pro | Tyr | Thr | Pro | Ser | Thr | Ala | Asp | Ile | Gln | Val | Ser | Asp |
|     |     |     | 20  |     |     |     |     | 25  |     |     |     |     | 30  |     |     |
| Asp | Asp | Lys | Ala | Gly | Ala | Thr | Leu | Leu | Phe | Ser | Gly | Ile | Phe | Leu | Gly |
|     |     | 35  |     |     |     |     | 40  |     |     |     |     | 45  |     |     |     |
| Leu | Val | Gly | Ile | Thr | Phe | Thr | Val | Met | Gly | Trp | Ile | Lys | Tyr | Gln | Gly |
|     | 50  |     |     |     |     | 55  |     |     |     |     | 60  |     |     |     |     |
| Val | Ser | His | Phe | Glu | Trp | Thr | Gln | Leu | Leu | Gly | Pro | Val | Leu | Leu | Ser |
| 65  |     |     |     |     | 70  |     |     |     |     | 75  |     |     |     |     | 80  |
| Val | Gly | Val | Thr | Phe | Ile | Leu | Ile | Ala | Val | Cys | Lys | Phe | Lys | Met | Leu |
|     |     |     |     | 85  |     |     |     |     | 90  |     |     |     |     | 95  |     |
| Ser | Cys | Gln | Leu | Cys | Lys | Glu | Ser | Glu | Glu | Arg | Val | Pro | Asp | Ser | Glu |
|     |     |     | 100 |     |     |     |     | 105 |     |     |     |     | 110 |     |     |
| Gln | Thr | Pro | G1y | Gly | Pro | Ser | Phe | Val | Phe | Thr | Gly | Ile | Asn | Gln | Pro |
|     |     | 115 |     |     |     |     | 120 |     |     |     |     | 125 |     |     |     |
| Ile | Thr | Phe | His | Gly | Ala | Thr | Val | Val | Gln | Tyr | Ile | Pro | Pro | Pro | Tyr |
|     | 130 |     |     |     |     | 135 |     |     |     |     | 140 |     |     |     |     |
| Gly | Ser | Pro | Glu | Pro | Met | Gly | Ile | Asn | Thr | Ser | Tyr | Leu | Gln | Ser | Val |
| 145 |     |     |     |     | 150 |     |     |     |     | 155 |     |     |     |     | 160 |
| Val | Ser | Pro | Cys | Gly | Leu | Ile | Thr | Ser | Gly | Gly | Ala | Ala | Ala | Ala | Met |
|     |     |     |     | 165 |     |     |     |     | 170 |     |     |     |     | 175 |     |
| Ser | Ser | Pro | Pro | Gln | Tyr | Tyr | Thr | Ile | Tyr | Pro | Gln | Asp | Asn | Ser | Ala |
|     |     |     | 180 | ı   |     |     |     | 185 |     |     |     |     | 190 | )   |     |
| Phe | Val | Val | Asp | Glu | Gly | Cys | Leu | Ser | Phe | Thr | Asp | Gly | Gly | Asn | His |
|     |     | 195 | ·   |     |     |     | 200 | ) / | شرو |     |     | 205 | 5   |     |     |

Arg Pro Asn Pro Asp Val Asp Gln Leu Glu Glu Thr Gln Leu Glu Glu Glu Ala Cys Ala Cys Phe Ser Pro Pro Pro Tyr Glu Glu Ile Tyr Ser Leu Pro Arg <210> 40 <211> 270 <212> PRT <213> Homo sapiens <400> 40 Met Ala Gly Ala Glu Asp Trp Pro Gly Gln Gln Leu Glu Leu Asp Glu Asp Glu Ala Ser Cys Cys Arg Trp Gly Ala Gln His Ala Gly Ala Arg Glu Leu Ala Ala Leu Tyr Ser Pro Gly Lys Arg Leu Gln Glu Trp Cys Ser Val Ile Leu Cys Phe Ser Leu Ile Ala His Asn Leu Val His Leu Leu Leu Ala Arg Trp Glu Asp Thr Pro Leu Val Ile Leu Gly Val Val Ala Gly Ala Leu Ile Ala Asp Phe Leu Ser Gly Leu Val His Trp Gly Ala Asp Thr Trp Gly Ser Val Glu Leu Pro Ile Val Gly Lys Ala

Phe Ile Arg Pro Phe Arg Glu His His Ile Asp Pro Thr Ala Ile Thr Arg His Asp Phe Ile Glu Thr Asn Gly Asp Asn Cys Leu Val Thr Leu Leu Pro Leu Leu Asn Met Ala Tyr Lys Phe Arg Thr His Ser Pro Glu Ala Leu Glu Gln Leu Tyr Pro Trp Glu Cys Phe Val Phe Cys Leu Ile Ile Phe Gly Thr Phe Thr Asn Gln Ile His Lys Trp Ser His Thr Tyr Phe Gly Leu Pro Arg Trp Val Thr Leu Leu Gln Asp Trp His Val Ile Leu Pro Arg Lys His His Arg Ile His His Val Ser Pro His Glu Thr Tyr Phe Cys Ile Thr Thr Gly Trp Leu Asn Tyr Pro Leu Glu Lys Ile Gly Phe Trp Arg Arg Leu Glu Asp Leu Ile Gln Gly Leu Thr Gly Glu Lys Pro Arg Ala Asp Asp Met Lys Trp Ala Gln Lys Ile Lys 

<210> 41

<211> 1131

<212> DNA

<213> Homo sapiens

⟨400⟩ 41

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|----------|-----|------------|------------|------------|------------|------------|------|
| agcactac | gc  | ggccgccttc | cacgcccgag | ggcatcgcgc | tggcctacgg | cagcctcctg | 120  |
| ctcatggc | gc  | tgctgcccat | cttcttcggc | gccctgcgct | ccgtacgctg | cgcccgcggc | 180  |
| aagaatgo | tt  | cagacatgcc | tgaaacaatc | accagccggg | atgccgcccg | cttccccatc | 240  |
| atcgccag | ct  | gcacactctt | ggggctctac | ctcttttca  | aaatattctc | ccaggagtac | 300  |
| atcaacct | сс  | tgctgtccat | gtatttcttc | gtgctgggaa | tcctggccct | gtcccacacc | 360  |
| atcagccc | ct  | tcatgaataa | gtttttcca  | gccagctttc | caaatcgaca | gtaccagctg | 420  |
| ctcttcac | ac  | agggttctgg | ggaaaacaag | gaagagatca | tcaattatga | atttgacacc | 480  |
| aaggacct | gg  | tgtgcctggg | cctgagcagc | atcgttggcg | tctggtacct | gctgaggaag | 540  |
| cactggat | tg  | ccaacaacct | ttttggcctg | gccttctccc | ttaatggagt | agagctcctg | 600  |
| cacctcaa | ca  | atgtcagcac | tggctgcatc | ctgctgggcg | gactcttcat | ctacgatgtc | 660  |
| ttctgggt | at  | ttggcaccaa | tgtgatggtg | acagtggcca | agtccttcga | ggcaccaata | 720  |
| aaattggt | gt  | ttccccagga | tctgctggag | aaaggcctcg | aagcaaacaa | ctttgccatg | 780  |
| ctgggact | tg  | gagatgtcgt | cattccaggg | atcttcattg | ccttgctgct | gcgctttgac | 840  |
| atcagctt | ga  | agaagaatac | ccacacctac | ttctacacca | gctttgcagc | ctacatcttc | 900  |
| ggcctggg | gcc | ttaccatctt | catcatgcac | atcttcaagc | atgctcagcc | tgccctccta | 960  |
| tacctggt | cc  | ccgcctgcat | cggttttcct | gtcctggtgg | cgctggccaa | gggagaagtg | 1020 |
| acagagat | gt  | tcagttatga | ggagtcaaat | cctaaggatc | cagcggcagt | gacagaatcc | 1080 |
| aaagaggg | gaa | cagaggcatc | agcatcgaag | gggctggaga | agaaagagaa | а          | 1131 |

⟨210⟩ 42

<211> 243

<212> DNA

بالإ

<213> Homo sapiens

<400> 42

atgacggcgc acteattege ceteceggte ateatettea ceaegttetg gggcetegte 60 ggcategeeg ggeeetggtt egtgeegaag ggacceaace geggagtgat cateaceatg 120 etggtegeea eegeegtetg etgttacete ttetggetea tegeeateet ggegeagetg 180 aaceeetgt tegggeecea getgaagaat gagaceatet ggtacgtgeg etteetgtgg 240 gag

⟨210⟩ 43

⟨211⟩ 1461

<212> DNA

<213> Homo sapiens

<400> 43

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| ccctggtga  | cggcgtgcta | catcctcatg | aacgtgtcct | acttcaccgt | gatgactgcc | 840  |
|------------|------------|------------|------------|------------|------------|------|
| accgaactcc | tgcagtccca | ggcggtggct | gtgacatttg | gtgaccgtgt | tctctatcct | 900  |
| gcttcttgga | tcgttccact | ttttgtggca | ttttcaacca | tcggtgctgc | taacgggacc | 960  |
| tgcttcacag | cgggcagact | catttacgtg | gcgggccggg | agggtcacat | gctcaaagtg | 1020 |
| ctttcttaca | tcagcgtcag | gcgcctcact | ccagcccccg | ccatcatctt | ttatggtatc | 1080 |
| atagcaacga | tttatatcat | ccctggtgac | ataaactcgt | tagtcaatta | tttcagcttt | 1140 |
| gccgcatggc | tgttttatgg | cctgacgatt | ctaggactca | tcgtgatgag | atttacaagg | 1200 |
| aaagagctgg | aaaggcctat | caaggtgccc | gtagtcattc | ccgtcttgat | gacactcatc | 1260 |
| tctgtgtttt | tggttctggc | tccaatcatc | agcaagccca | cctgggagta | cctctactgt | 1320 |
| gtgctgttta | tattaagcgg | ccttttattt | tacttcctgt | ttgtccacta | caagtttgga | 1380 |
| tgggctcaga | aaatctcaaa | gccgattacc | atgcaccttc | agatgctaat | ggaagtggtc | 1440 |
| ccaccggagg | aagaccctga | g          |            |            |            | 1461 |

⟨210⟩ 44

<211> 1125

<212> DNA

<213> Homo sapiens

<400> 44

| ä | atgacccccc | agcccgccgg | accccggat  | gggggctggg | gctgggtggt | ggcggccgca | 60  |
|---|------------|------------|------------|------------|------------|------------|-----|
| 8 | gccttcgcga | taaacgggct | gtcctacggg | ctgctgcgct | cgctgggcct | tgccttccct | 120 |
| 1 | gaccttgccg | agcactttga | ccgaagcgcc | caggacactg | cgtggatcag | cgccctggcc | 180 |
| ( | ctggccgtgc | agcaggcagc | cagccccgtg | ggcagcgccc | tgagcacgcg | ctggggggcc | 240 |
| ( | cgccccgtgg | tgatggttgg | gggcgtcctc | gcctcgctgg | gcttcgtctt | ctcggctttc | 300 |
| 1 | gccagcggtc | tgctgcatct | ctacctcggc | ctgggcctcc | tcgctggctt | tggttgggcc | 360 |
| • | ctggtgttcg | ccccgccct  | aggcaccctc | tcgcgttact | tctcccgccg | tcgagtcttg | 420 |

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| 480  | gcccgccttg | tgctcctggc | gcctcctcgc | cggcaacggg | tggcgctcac | gcggtggggc |
|------|------------|------------|------------|------------|------------|------------|
| 540  | cgcgatcacc | tcctcctcgg | ggcgctctgc | cggctggcgg | tcgatacttt | cagcttctcc |
| 600  | agacccccca | tccttcctgg | ctacccctgg | cgccctgctg | cccctgtgg  | ctccacctca |
| 660  | ccgggccttc | tgttcacacg | ggcctgagtc | agctgccctc | gtagtcccct | gcccaccgc  |
| 720  | ttacgtgcac | acttcgttcc | gggggcgggt | agccctggtt | ctctaggcac | tcaatctttg |
| 780  | tggtggccgt | gcagcgctgg | gggatacgga | ggggcctggg | gctttagacc | ttggctcccc |
| 840  | accaaggctg | tggctggcag | ggtctgcggg | gcgcccggct | ggggatgcgg | ggctgcgatg |
| 900  | ggctgtgggt | actgggctgg | cggggctctg | tggccgtatt | ccgcggctgc | ggtgcccctc |
| 960  | tgctggccgc | gggggtcccc | agagagctgg | tgggcggcga | gtgcccgtgg | ggtggggctg |
| 1020 | gtgtactccc | ctggttttcg | ttacgccccg | gcgcggggag | tatgggctga | ggctgtggcc |
| 1080 | tgctgatgag | ctggtgatga | ggccacaggg | gtgtggtgca | ggcgtcggag | cgggctggtg |
| 1125 |            | aggga      | aggcttccta | ctccctgtc  | ctcctgggcc | cctcgggggg |

⟨210⟩ 45

<211> 1050

<212> DNA

<213> Homo sapiens

<400> 45

| aagatggtca | acttccccca | gaaaattgca | ggtgaactct | atggacctct | catgctggtc | 480  |
|------------|------------|------------|------------|------------|------------|------|
| ttcactctgg | ttgctatcct | actccatggg | atgaagacgt | ctgacactat | tatccgggag | 540  |
| ggcaccctga | tgggcacagc | cattggcacc | tgcttcggct | actggctggg | agtctcatcc | 600  |
| ttcatttact | tccttgccta | cctgtgcaac | gcccagatca | ccatgctgca | gatgttggca | 660  |
| ctgctgggct | atggcctctt | tgggcattgc | attgtcctgt | tcatcaccta | taatatccac | 720  |
| ctccacgccc | tcttctacct | cttctggctg | ttggtgggtg | gactgtccac | actgcgcatg | 780  |
| gtagcagtgt | tggtgtctcg | gaccgtgggc | cccacacagc | ggctgctcct | ctgtggcacc | 840  |
| ctggctgccc | tacacatgct | cttcctgctc | tatctgcatt | ttgcctacca | caaagtggta | 900  |
| gaggggatcc | tggacacact | ggagggcccc | aacatcccgc | ccatccagag | ggtccccaga | 960  |
| gacatccctg | ccatgctccc | tgctgctcgg | cttcccacca | ccgtcctcaa | cgccacagcc | 1020 |
| aaagctgttg | cggtgaccct | gcagtcacac |            |            |            | 1050 |

⟨210⟩ 46

<211> 2001

<212> DNA

<213> Homo sapiens

<400> 46

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| ctggctgcct | gtgccacggc   | tggccacaca | gctgcacacc         | tgctcggcag | cacgctgtcc | 540  |
|------------|--------------|------------|--------------------|------------|------------|------|
| tgggcccacc | ttggggtcca   | ggtctggcag | agggcagagt         | gtccccaggt | gcccaagatc | 600  |
| tacaagtact | actccctgct   | ggcctccctg | cctctcctgc         | tgggcctcgg | attcctgagc | 660  |
| ctttggtacc | ctgtgcagct   | ggtgagaagc | ttcagccgta         | ggacaggagc | aggctccaag | 720  |
| gggctgcaga | gcagctactc   | tgaggaatat | ctgaggaacc         | tcctttgcag | gaagaagctg | 780  |
| ggaagcagct | accacacctc   | caagcatggc | ttcctgtcct         | gggcccgcgt | ctgcttgaga | 840  |
| cactgcatct | acactccaca   | gccaggattc | catctcccgc         | tgaagctggt | gctttcagct | 900  |
| acactgacag | ggacggccat   | ttaccaggtg | gccctgctgc         | tgctggtggg | cgtggtaccc | 960  |
| actatccaga | aggtgagggc   | aggggtcacc | acggatgtct         | cctacctgct | ggccggcttt | 1020 |
| ggaatcgtgc | tctccgagga   | caagcaggag | gtggtggagc         | tggtgaagca | ccatctgtgg | 1080 |
| gctctggaag | tgtgctacat   | ctcagccttg | gtcttgtcct         | gcttactcac | cttcctggtc | 1140 |
| ctgatgcgct | cactggtgac   | acacaggacc | aaccttcgag         | ctctgcaccg | aggagetgee | 1200 |
| ctggacttga | gtcccttgca   | tcggagtccc | catccctccc         | gccaagccat | attctgttgg | 1260 |
| atgagcttca | gtgcctacca   | gacagccttt | atctgccttg         | ggctcctggt | gcagcagatc | 1320 |
| atcttcttcc | tgggaaccac   | ggccctggcc | ttcctggtgc         | tcatgcctgt | gctccatggc | 1380 |
| aggaacctcc | tgctcttccg   | ttccctggag | tcctcgtggc         | ccttctggct | gactttggcc | 1440 |
| ctggctgtga | tcctgcagaa   | catggcagcc | cattgggtct         | tcctggagac | tcatgatgga | 1500 |
| cacccacago | tgaccaaccg   | gcgagtgctc | tatgcagcca         | cctttcttct | cttcccctc  | 1560 |
| aatgtgctgg | tgggtgccat   | ggtggccacc | tggcgagtgc         | tcctctctgc | cctctacaac | 1620 |
| gccatccacc | ttggccagat   | ggacctcagc | ctgctgccac         | cgagagccgc | cactetegae | 1680 |
| cccggctact | acacgtaccg   | aaacttcttg | aagattgaag         | tcagccagtc | gcatccagcc | 1740 |
| atgacagcct | tctgctccct   | gctcctgcaa | gcgcagagcc         | tcctacccag | gaccatggca | 1800 |
| gcccccagg  | gacagcctcag  | accaggggag | gaagacgaag         | ggatgcagct | gctacagaca | 1860 |
| aaggactcca | tggccaaggg   | agctaggcco | ggggccagcc .<br>نر | gcggcagggc | tcgctggggt | 1920 |
| ctggcctaca | a cgctgctgca | caacccaacc | ctgcaggtct         | tccgcaagac | ggccctgttg | 1980 |

ggtgccaatg gtgcccagcc c

2001

<210> 47

⟨211⟩ 1392

<212> DNA

<213> Homo sapiens

<400> 47

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| tcgcctttgt | ctaacaggtt | ccgagtggtt | gcccgaagca | tggctgcctt | cctttcagtt | 1140 |
|------------|------------|------------|------------|------------|------------|------|
| caggttccta | tggaagatca | gatccgtttg | aggcctggct | ctgaattaca | tctgaccccc | 1200 |
| aaagctcagc | aggctctgaa | tgctcttgaa | tccatggcat | caagtaagca | gtatgttgaa | 1260 |
| taccaggatc | aaatattgca | agccacccaa | tttataaggc | atcctggcca | ttgccttcaa | 1320 |
| gatgggaaaa | gcttcttggc | tcttctcgtt | aactgtctgt | atccagaagt | gcattatttg | 1380 |
| gaccacatac | ga         |            |            |            |            | 1392 |

⟨210⟩ 48

<211> 1410

<212> DNA

<213> Homo sapiens

**<400>** 48

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| cagctgctgc | tcaacaacaa | gctggtgtat | ggaagccggc | aggactttct | ctggcgcctg | 840  |
|------------|------------|------------|------------|------------|------------|------|
| gcccgagcct | acagtgacat | gtgtgagctc | actgaggagg | tgagcgagaa | gaagtcatat | 900  |
| gccctagatg | gaaaagaaga | agcagaggct | gctctggaga | agggggatga | gagtgctgac | 960  |
| tgtcacctgt | ggtatgcggt | gctttgtggt | cagctggctg | agcatgagag | catccagagg | 1020 |
| cgcatccaga | gtggctttag | cttcaaggag | catgtggaca | aagccattgc | tctccagcca | 1080 |
| gaaaacccca | tggctcactt | tcttcttggc | aggtggtgct | atcaggtctc | tcacctgagc | 1140 |
| tggctagaaa | aaaaaactgc | tacagccttg | cttgaaagcc | ctctcagtgc | cactgtggaa | 1200 |
| gatgccctcc | agagetteet | aaaggctgaa | gaactacagc | caggattttc | caaagcagga | 1260 |
| agggtatata | tttccaagtg | ctacagagaa | ctagggaaaa | actctgaagc | tagatggtgg | 1320 |
| atgaagttgg | ccctggagct | gccagatgtc | acgaaggagg | atttggctat | ccagaaggac | 1380 |
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#### 98 / 307

| gtgagcccct | gcggcctcat | aacctctgga | ggggcagcag | ccgccatgtc | aagtcctcct | 540 |
|------------|------------|------------|------------|------------|------------|-----|
| caatactaca | ccatctaccc | tcaagataac | tctgcatttg | tggttgatga | gggctgcctt | 600 |
| tctttcacgg | acggtggaaa | tcacaggccc | aatcctgatg | ttgaccagct | agaagagaca | 660 |
| cagctggaag | aggaggcctg | tgcctgcttc | tetectecee | cttatgaaga | aatatactct | 720 |
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⟨211⟩ 810

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| caag | gggg  | aac g | gtggo | ettte | ec ct | tgcag | gagco | ggt   | tgtct | ccg | cctg  | cgt | cc 1 | tgct  | gcagca | 60  |
| acce | gago  | ctg g | gagto | eggat | c co  | cgaad | egcad | c cct | tege  | ate | g gad | tce | gco  | cto   | c agc  | 115 |
|      |       |       |       |       |       |       |       |       |       | Met | t Asp | Sei | Ala  | a Lei | ı Ser  |     |
|      |       |       |       |       |       |       |       |       |       | ]   | l     |     |      |       | 5      |     |
| gat  | ccg   | cat   | aac   | ggc   | agt   | gcc   | gag   | gca   | ggc   | ggc | ccc   | acc | aac  | agc   | act    | 163 |
| Asp  | Pro   | His   | Asn   | Gly   | Ser   | Ala   | Glu   | Ala   | Gly   | Gly | Pro   | Thr | Asn  | Ser   | Thr    |     |
|      |       |       | 10    |       |       |       |       | 15    |       |     |       |     | 20   |       |        |     |
| acg  | cgg   | ccg   | cct   | tcc   | acg   | ccc   | gag   | ggc   | atc   | gcg | ctg   | gcc | tac  | ggc   | agc    | 211 |
| Thr  | Arg   | Pro   | Pro   | Ser   | Thr   | Pro   | Glu   | Gly   | Ile   | Ala | Leu   | Ala | Tyr  | Gly   | Ser    |     |
|      |       | 25    |       |       |       |       | 30    |       |       |     |       | 35  |      |       |        |     |
| ctc  | ctg   | ctc   | atg   | gcg   | ctg   | ctg   | ccc   | atc   | ttc   | ttc | ggc   | gcc | ctg  | cgc   | tcc    | 259 |
| Leu  | Leu   | Leu   | Met   | Ala   | Leu   | Leu   | Pro   | Ile   | Phe   | Phe | Gly   | Ala | Leu  | Arg   | Ser    |     |
|      | 40    |       |       |       |       | 45    |       |       |       |     | 50    |     |      |       |        |     |
| gta  | cgc   | tgc   | gcc   | cgc   | ggc   | aag   | aat   | gct   | tca   | gac | atg   | cct | gaa  | aca   | atc    | 301 |
| Val  | Arg   | Cys   | Ala   | Arg   | Gly   | Lys   | Asn   | Ala   | Ser   | Asp | Met   | Pro | Glu  | Thr   | Ile    |     |
| 55   |       |       |       |       | 60    |       |       |       |       | 65  |       |     |      |       | 70     |     |

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| acc | agc | cgg | gat | gcc | gcc | cgc | ttc | ccc | atc  | atc | gcc | agc | tgc   | aca | ctc | 355 |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|------|-----|-----|-----|-------|-----|-----|-----|
| Thr | Ser | Arg | Asp | Ala | Ala | Arg | Phe | Pro | Ile  | Ile | Ala | Ser | Cys   | Thr | Leu |     |
|     |     |     |     | 75  |     |     |     |     | 80   |     |     |     |       | 85  |     |     |
| ttg | ggg | ctc | tac | ctc | ttt | ttc | aaa | ata | ttc  | tcc | cag | gag | tac   | atc | aac | 403 |
| Leu | Gly | Leu | Tyr | Leu | Phe | Phe | Lys | Ile | Phe  | Ser | Gln | Glu | Tyr   | Ile | Asn |     |
|     |     |     | 90  |     |     |     |     | 95  |      |     |     |     | 100   |     | •   |     |
| ctc | ctg | ctg | tcc | atg | tat | ttc | ttc | gtg | ctg  | gga | atc | ctg | gcc   | ctg | tcc | 451 |
| Leu | Leu | Leu | Ser | Met | Tyr | Phe | Phe | Val | Leu  | Gly | Ile | Leu | Ala   | Leu | Ser |     |
|     |     | 105 |     |     |     |     | 110 |     |      |     |     | 115 |       |     |     |     |
| cac | acc | atc | agc | ccc | ttc | atg | aat | aag | ttt  | ttt | cca | gcc | agc   | ttt | cca | 499 |
| His | Thr | Ile | Ser | Pro | Phe | Met | Asn | Lys | Phe  | Phe | Pro | Ala | Ser   | Phe | Pro |     |
|     | 120 |     |     |     |     | 125 |     |     |      |     | 130 |     | ,     |     |     |     |
| aat | cga | cag | tac | cag | ctg | ctc | ttc | aca | cag  | ggt | tct | ggg | gaa   | aac | aag | 547 |
| Asn | Arg | Gln | Tyr | Gln | Leu | Leu | Phe | Thr | Gln  | Gly | Ser | Gly | Glu   | Asn | Lys |     |
| 135 |     |     |     |     | 140 |     |     |     |      | 145 |     |     |       |     | 150 |     |
| gaa | gag | atc | atc | aat | tat | gaa | ttt | gac | acc  | aag | gac | ctg | gtg   | tgc | ctg | 595 |
| Glu | Glu | Ile | Ile | Asn | Tyr | Glu | Phe | Asp | Thr  | Lys | Asp | Leu | Val   | Cys | Leu |     |
|     |     |     |     | 155 |     |     |     |     | 160  |     |     |     |       | 165 |     |     |
| ggc | ctg | agc | agc | atc | gtt | ggc | gtc | tgg | tac  | ctg | ctg | agg | aag   | cac | tgg | 643 |
| Gly | Leu | Ser | Ser | Ile | Val | Gly | Val | Trp | Tyr  | Leu | Leu | Arg | Lys   | His | Trp |     |
|     |     |     | 170 |     |     |     |     | 175 |      |     |     |     | 180   |     |     |     |
| att | gcc | aac | aac | ctt | ttt | ggc | ctg | gcc | ttc  | tcc | ctt | aat | gga.  | gta | gag | 691 |
| Ile | Ala | Asn | Asn | Leu | Phe | Gly | Leu | Ala | Phe  | Ser | Leu | Asr | Gly   | Val | Glu |     |
|     |     | 185 |     |     |     |     | 190 | •   | نتسق |     |     | 195 | 5     |     |     |     |
| cto | ctg | cac | ctc | aac | aat | gto | ago | act | ggc  | tgo | ato | ctg | g ctg | gge | gga | 739 |

| Leu | Leu | His | Leu | Asn | Asn | Val | Ser | Thr | Gly | Cys | Ile | Leu | Leu | Gly | Gly |      |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|------|
|     | 200 |     |     |     |     | 205 |     |     |     |     | 210 |     |     |     |     |      |
| ctc | ttc | atc | tac | gat | gtc | ttc | tgg | gta | ttt | ggc | acc | aat | gtg | atg | gtg | 787  |
| Leu | Phe | Ile | Tyr | Asp | Val | Phe | Trp | Val | Phe | Gly | Thr | Asn | Val | Met | Val |      |
| 215 |     |     |     |     | 220 |     |     |     |     | 225 |     |     |     |     | 230 |      |
| aca | gtg | gcc | aag | tcc | ttc | gag | gca | cca | ata | aaa | ttg | gtg | ttt | ссс | cag | 835  |
| Thr | Val | Ala | Lys | Ser | Phe | Glu | Ala | Pro | Ile | Lys | Leu | Val | Phe | Pro | G1n |      |
|     |     |     |     | 235 |     |     |     |     | 240 | •   |     |     |     | 245 |     |      |
| gat | ctg | ctg | gag | aaa | ggc | ctc | gaa | gca | aac | aac | ttt | gcc | atg | ctg | gga | 883  |
| Asp | Leu | Leu | Glu | Lys | Gly | Leu | Glu | Ala | Asn | Asn | Phe | Ala | Met | Leu | Gly |      |
|     |     |     | 250 |     |     |     |     | 255 |     |     |     |     | 260 |     |     |      |
| ctt | gga | gat | gtc | gtc | att | cca | ggg | atc | ttc | att | gcc | ttg | ctg | ctg | cgc | 931  |
| Leu | Gly | Asp | Val | Val | Ile | Pro | Gly | Ile | Phe | Ile | Ala | Leu | Leu | Leu | Arg |      |
|     |     | 265 |     |     |     |     | 270 |     |     |     |     | 275 |     |     |     |      |
| ttt | gac | atc | agc | ttg | aag | aag | aat | acc | cac | acc | tac | ttc | tac | acc | agc | 979  |
| Phe | Asp | Ile | Ser | Leu | Lys | Lys | Asn | Thr | His | Thr | Tyr | Phe | Tyr | Thr | Ser |      |
|     | 280 |     |     |     |     | 285 |     |     |     |     | 290 |     |     |     |     |      |
| ttt | gca | gcc | tac | atc | ttc | ggc | ctg | ggc | ctt | acc | atc | ttc | atc | atg | cac | 1027 |
| Phe | Ala | Ala | Tyr | Ile | Phe | Gly | Leu | Gly | Leu | Thr | Ile | Phe | Ile | Met | His |      |
| 295 |     |     |     |     | 300 |     |     |     |     | 305 |     |     |     |     | 310 |      |
| atc | ttc | aag | cat | gct | cag | cct | gcc | ctc | cta | tac | ctg | gtc | ccc | gcc | tgc | 1075 |
| Ile | Phe | Lys | His | Ala | Gln | Pro | Ala | Leu | Leu | Tyr | Leu | Val | Pro | Ala | Cys |      |
|     |     |     |     | 315 |     |     |     |     | 320 |     |     |     |     | 325 |     |      |
| atc | ggt | ttt | cct | gtc | ctg | gtg | gcg | ctg | gcc | aag | gga | gaa | gtg | aca | gag | 1123 |
| Ile | Gly | Phe | Pro | Val | Leu | Val | Ala | Leu | Ala | Lys | Gly | Glu | Val | Thr | Glu |      |

|      |      |       | 330   |       |      |       |       | 335   |       |       |      |       | 340   |       |        |     |    |
|------|------|-------|-------|-------|------|-------|-------|-------|-------|-------|------|-------|-------|-------|--------|-----|----|
| atg  | ttc  | agt   | tat   | gag   | gag  | tca   | aat   | cct   | aag   | gat   | cca  | gcg   | gca   | gtg   | aca    | 117 | 1  |
| Met  | Phe  | Ser   | Tyr   | Glu   | Glu  | Ser   | Asn   | Pro   | Lys   | Asp   | Pro  | Ala   | Ala   | Val   | Thr    |     |    |
|      |      | 345   |       |       |      |       | 350   |       |       |       |      | 355   |       |       |        |     |    |
| gaa  | tcc  | aaa   | gag   | gga   | aca  | gag   | gca   | tca   | gca   | tcg   | aag  | ggg   | ctg   | gag   | aag    | 121 | 9  |
| Glu  | Ser  | Lys   | Glu   | Gly   | Thr  | Glu   | Ala   | Ser   | Ala   | Ser   | Lys  | Gly   | Leu   | Glu   | Lys    |     |    |
|      | 360  |       |       |       |      | 365   |       |       |       |       | 370  |       |       |       |        |     |    |
| aaa  | gag  | aaa   | tg a  | atgca | agct | gg t  | gcccg | gagco | tc1   | tcagg | ggcc | agad  | ccag  | aca   |        | 127 | '0 |
| Lys  | Glu  | Lys   |       |       |      |       |       |       |       |       |      |       | •     |       |        |     |    |
| 375  |      |       |       |       |      |       |       |       |       |       |      |       |       |       |        |     |    |
| gat  | gggg | gct ( | gggc  | ccaca | ac a | ggcgi | tgcad | c cgs | gtaga | aggg  | caca | aggag | ggc ( | caag  | ggcagc | 133 | 0  |
| tcc  | agga | cag ( | ggca  | gggg  | gc a | gcag  | gatad | cto   | cago  | ccag  | gcct | tctg  | tgg ( | cctci | tgtttc | 139 | 0  |
| ctt  | ctcc | ctt   | tcttį | ggcc  | ct c | ctct  | gctc  | c tco | cca   | cacc  | ctgo | caggo | caa a | aagaa | aacccc | 145 | 0  |
| cage | cttc | ccc ( | cctc  | cccg  | gg a | gccas | ggtgg | g gaa | aaagt | ggg   | tgtg | gatti | ttt a | agati | ttgta  | 151 | 0  |
| ttg  | tgga | ctg   | attti | tgcci | tc a | catta | aaaaa | a cto | catco | ccat  | g    |       |       |       |        | 155 | 1  |
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|------|------|-------|-------|-------|-------|------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|
|      |      |       |       |       |       |      | . 1   | let 1 | Thr A | Ala H | dis S | Ser l | Phe . | Ala I | Leu   |       |
|      |      |       | ,     |       |       | ••   |       | 1     |       |       |       | 5     |       |       |       |       |
| ccg  | gtc  | atc   | atc   | ttc   | acc   | acg  | ttc   | tgg   | ggc   | ctc   | gtc   | ggc   | atc   | gcc   | ggg   | 160   |
| Pro  | Val  | Ile   | Tle   | Phe   | Thr   | Thr  | Phe   | Trp   | Gly   | Leu   | Val   | Gly   | Ile   | Ala   | Gly   |       |
|      | 10   |       |       |       |       | 15   |       |       |       |       | 20    |       |       |       |       |       |
| ссс  | tgg  | ttc   | gtg   | ccg   | aag   | gga  | ССС   | aac   | cgc   | gga   | gtg   | atc   | atc   | acc   | atg   | 208   |
| Pro  | Trp  | Phe   | Val   | Pro   | Lys   | Gly  | Pro   | Asn   | Arg   | Gly   | Val   | Ile   | Ile   | Thr   | Met   |       |
| 25   |      |       |       |       | 30    |      |       |       |       | 35    |       |       |       |       | 40    |       |
| ctg  | gtc  | gcc   | acc   | gcc   | gtc   | tgc  | tgt   | tac   | ctc   | ttc   | tgg   | ctc   | atc   | gcc   | atc   | 256   |
| Leu  | Val  | Ala   | Thr   | Ala   | Val   | Cys  | Cys   | Tyr   | Leu   | Phe   | Trp   | Leu   | Ile   | Ala   | Ile   |       |
|      |      |       |       | 45    |       |      |       | •     | 50    |       |       |       |       | 55    |       |       |
| ctg  | gcg  | cag   | ctg   | aac   | ссс   | ctg  | ttc   | ggg   | ссс   | cag   | ctg   | aag   | aat   | gag   | acc   | 304   |
| Leu  | Ala  | Gln   | Leu   | Asn   | Pro   | Leu  | Phe   | Gly   | Pro   | Gln   | Leu   | Lys   | Asn   | Glu   | Thr   |       |
|      |      |       | 60    |       |       |      |       | 65    |       |       |       |       | 70    |       |       |       |
| atc  | tgg  | tac   | gtg   | cgc   | ttc   | ctg  | tgg   | gag   | tga   | cccg  | cc g  | ccc   | cgac  | с     |       | 350   |
| Ile  | Trp  | Tyr   | Val   | Arg   | Phe   | Leu  | Trp   | Glu   |       |       |       |       |       |       |       |       |
|      |      | 75    |       |       |       |      | 80    |       |       |       |       |       |       |       |       |       |
| cag  | gtgc | cca   | gctc  | tcgg  | aa t  | gact | gtgg  | c to  | cact  | gtcc  | ctg   | acaa  | ссс   | cttc  | gtccg | g 410 |
| acc  | ctcc | ccc   | acac  | aact  | at g  | tctg | gtca  | c ca  | gctc  | cctc  | ctg   | ctgg  | cac   | ccag  | agacc | c 470 |
| gga  | cccg | cag   | ggcc  | tgcc  | tg g  | ttcc | tgga  | a gt  | cttc  | ccag  | tct   | tccc  | agc   | cagc  | ccggg | c 530 |
| cct  | gggg | agc   | cctg  | ggca  | ca g  | cago | ggcc  | g ag  | ggga  | tgtc  | ctg   | ctcc  | aat   | accc  | gcact | g 590 |
| ctc  | tgga | gtt   | tgcc  | ctct  | tt c  | ccaa | ggag  | a tg  | ctgc  | tggg  | gag   | ctgg  | tat   | gggt  | ggggt | c 650 |
| ttt  | ccct | tta   | caga  | cggg  | gc a  | gatg | ccag  |       | tçag  | ccca  | tcc   | tgag  | gag   | gaca  | cgtgt | c 710 |
| ctc  | atgg | aga   | gggt  | gctc  | cg g  | ccca | ggcg  | g gg  | gagt  | cagt  | gcc   | cagt  | cag   | cago  | tctgc | c 770 |

| accatcctgc | tgggaactgg | gggggcctct | attgggttat | aggcaaggcc | ttttctctgg | 830  |
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| catggaattg | ttaattttct | gacacgtcta | gatgtgaaat | ttctgaaaat | gttgaagcag | 890  |
| agaaacattc | acacacaaaa | agcaacatag | tcatgtgggt | ccagatggcc | tcagtcctag | 950  |
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| cagcatctaa | gtgaccagag | ctgggatgag | agagggaag  | gggcaatgtg | agtggcgcta | 1190 |
| tgggacgggc | cagccctgct | cctgagccag | ccccgccctc | tgcccctgg  | ccctgggctc | 1250 |
| tgtgctaggg | atggtgaaga | atgggggcgt | gccagcctgg | caggagtggg | aagcaacacg | 1310 |
| caggggtccc | ggacctctcc | agccttgccc | tcacgcttac | ccgagctccc | agtgtggtta | 1370 |
| gcacagagct | cacccacctt | gcctggctcc | cagctggggc | ctgtcctcac | tggtgctcca | 1430 |
| ggggaagaaa | cgacagcctc | acttctgtat | ggactgctga | tgtggcctgc | catcctgttc | 1490 |
| agcgggcatt | gtctttggag | cagcaggaga | ataggatgcc | tctcactcac | atgccagttc | 1550 |
| ctggctggcc | agctgctcag | ggctcaggct | ggggcctccc | attgacatcc | tcccctaca  | 1610 |
| ctccctctct | gagcctccgt | cgcccctcct | gttgggtaag | ggtgttgagt | gtgacttgtg | 1670 |
| ctgaaaacct | ggttcatata | taataaataa | tggtgatgaa | аад        |            | 1713 |

⟨210⟩ 53

<211> 1758

<212> DNA

<213> Homo sapiens

<220>

<221> CDS

⟨222⟩ (190)...(1653)

<400> 53

| ttto | ctagg | ggt 1 | tggad | ccgt  | gc ag | ggcad | cggg  | c ggt | tcago | ctgg  | gcc   | gcag  | ctc   | ctcc  | ggctc | t 60  |
|------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|
| gcag | gggto | cac g | ggagg | gaago | cc ag | gctco | ccta  | a gto | cag   | gccg  | agct  | ttgc  | act 1 | tgcg  | tcttg | t 120 |
| ctg  | etget | tgc 1 | tgaad | ccaa  | ga ti | ttago | etgt  | g cgo | cct   | cctt  | gcag  | gtct  | cct ( | ggaa  | ccago | a 180 |
| ggag | gaaa  | ac at | tg gg | gg ga | at a  | ct gg | gc c  | tg ag | ga aa | ag c  | gg ag | ga ga | ag ga | at ga | ag    | 228   |
|      |       | Me    | et G  | ly As | sp Tl | nr G  | ly Le | eu Ai | rg Ly | ys Aı | rg Aı | rg G  | lu As | sp G  | lu    |       |
|      |       |       | 1     |       |       |       | 5     |       |       |       | ]     | 10    |       |       |       |       |
| aag  | tcg   | atc   | cag   | agc   | caa   | gag   | cct   | aag   | acc   | acc   | agt   | ctc   | caa   | aag   | gag   | 276   |
| Lys  | Ser   | Ile   | Gln   | Ser   | Gln   | Glu   | Pro   | Lys   | Thr   | Thr   | Ser   | Leu   | Gln   | Lys   | Glu   |       |
|      | 15    |       |       |       |       | 20    |       |       |       |       | 25    |       |       |       |       |       |
| ctg  | ggc   | ctc   | atc   | agt   | ggc   | atc   | tcc   | atc   | atc   | gtg   | ggc   | acc   | atc   | att   | ggc   | 324   |
| Leu  | Gly   | Leu   | Ile   | Ser   | Gly   | Ile   | Ser   | Ile   | Ile   | Val   | Gly   | Thr   | Ile   | Ile   | Gly   |       |
| 30   | ·     |       |       |       | 35    |       |       |       |       | 40    |       |       |       |       | 45    |       |
| tct  | ggg   | atc   | ttc   | gtt   | tcc   | ccc   | aag   | tct   | gtg   | ctc   | agc   | aac   | acg   | gaa   | gct   | 372   |
| Ser  | Gly   | Ile   | Phe   | Val   | Ser   | Pro   | Lys   | Ser   | Val   | Leu   | Ser   | Asn   | Thr   | Glu   | Ala   |       |
|      |       |       |       | 50    |       |       |       |       | 55    |       |       |       |       | 60    |       |       |
| gtg  | ggg   | ccc   | tgc   | ctc   | atc   | ata   | tgg   | gcg   | gct   | tgc   | ggg   | gtc   | ctc   | gcg   | acg   | 420   |
| Val  | Gly   | Pro   | Cys   | Leu   | Ile   | Ile   | Trp   | Ala   | Ala   | Cys   | Gly   | Val   | Leu   | Ala   | Thr   |       |
|      |       |       | 65    |       |       |       |       | 70    |       |       |       |       | 75    |       |       |       |
| ctg  | ggt   | gcc   | ctg   | tgc   | ttt   | gcg   | gag   | ctt   | ggc   | aca   | atg   | atc   | acc   | aag   | tca   | 468   |
| Leu  | Gly   | Ala   | Leu   | Cys   | Phe   | Ala   | Glu   | Leu   | Gly   | Thr   | Met   | Ile   | Thr   | Lys   | Ser   |       |
|      |       | 80    |       |       |       |       | 85    |       |       |       |       | 90    |       |       |       |       |
| ggg  | gga   | gag   | tat   | ccc   | tac   | ctg   | atg   | gag   | gcc   | tac   | ggg   | ccc   | atc   | ccc   | gcc   | 516   |
| Gly  | Gly   | Glu   | Tyr   | Pro   | Tyr   | Leu   | Met   | Glu   | Ala   | Tyr   | Gly   | Pro   | Ile   | Pro   | Ala   |       |
|      | 95    |       |       |       |       | 100   |       |       | **نشو |       | 105   |       |       |       |       |       |
| tac  | ctc   | ttc   | tcc   | tgg   | gcc   | agc   | ctg   | atc   | gtc   | att   | aag   | ccc   | acg   | tcc   | ttc   | 564   |

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| Tyr | Leu | Phe | Ser   | Trp | Ala | Ser | Leu | Ile | Val       | Ile | Lys | Pro | Thr | Ser | Phe |     |
|-----|-----|-----|-------|-----|-----|-----|-----|-----|-----------|-----|-----|-----|-----|-----|-----|-----|
| 110 |     |     |       |     | 115 |     |     |     |           | 120 |     |     |     |     | 125 |     |
| gcc | atc | atc | tgc   | ctc | agc | ttc | tcc | gag | tat       | gtg | tgt | gcg | ccc | ttc | tat | 612 |
| Ala | Ile | Ile | Cys   | Leu | Ser | Phe | Ser | Glu | Tyr       | Val | Cys | Ala | Pro | Phe | Tyr |     |
|     |     |     |       | 130 |     |     |     |     | 135       |     |     |     |     | 140 |     |     |
| gtg | ggc | tgc | aag   | cct | cct | caa | atc | gtt | gtg       | aaa | tgc | ctg | gcc | gcc | gcc | 660 |
| Val | Gly | Cys | Lys   | Pro | Pro | Gln | Ile | Val | Val       | Lys | Cys | Leu | Ala | Ala | Ala |     |
|     |     |     | 145   |     |     |     |     | 150 |           |     |     |     | 155 |     |     |     |
| gcc | atc | ttg | ttc   | atc | tcg | aca | gtg | aac | tca       | ctg | agc | gtg | cgg | ctg | gga | 708 |
| Ala | Ile | Leu | Phe   | Ile | Ser | Thr | Val | Asn | Ser       | Leu | Ser | Val | Arg | Leu | Gly |     |
|     |     | 160 |       |     |     |     | 165 |     |           |     |     | 170 |     |     |     |     |
| agc | tac | gtc | cag   | aac | atc | ttc | acc | gcg | gcc       | aag | ctg | gtg | atc | gtg | gcc | 756 |
| Ser | Tyr | Val | Gln   | Asn | Ile | Phe | Thr | Ala | Ala       | Lys | Leu | Val | Ile | Val | Ala |     |
|     | 175 |     |       |     |     | 180 |     |     |           |     | 185 |     |     |     |     |     |
| atc | atc | atc | atc   | agc | ggg | ctg | gtg | ctc | ctg       | gcc | caa | gga | aac | aca | aag | 804 |
| Ile | Ile | Ile | Ile   | Ser | Gly | Leu | Val | Leu | Leu       | Ala | Gln | Gly | Asn | Thr | Lys |     |
| 190 |     |     |       |     | 195 |     |     |     |           | 200 |     |     |     |     | 205 |     |
| aat | ttt | gat | aat   | tct | ttc | gag | ggc | gcc | cag       | ctg | tct | gtg | gga | gcc | atc | 852 |
| Asn | Phe | Asp | Asn   | Ser | Phe | Glu | Gly | Ala | Gln       | Leu | Ser | Val | Gly | Ala | Ile |     |
|     |     |     |       | 210 | )   |     |     |     | 215       |     |     |     |     | 220 |     |     |
| agc | ctg | gcg | ttt   | tac | aat | gga | ctc | tgg | gcc       | tat | gat | gga | tgg | aat | caa | 900 |
| Ser | Leu | Ala | Phe   | Tyr | Asn | Gly | Leu | Trp | Ala       | Tyr | Asp | Gly | Trp | Asn | Gln |     |
|     |     |     | 225   |     |     |     |     | 230 |           |     |     |     | 235 | i   |     |     |
| ctc | aat | tac | atc   | aca | gaa | gaa | ctt | aga | aac<br>نر | cct | tac | aga | aac | ctg | cct | 948 |
| Leu | Asr | Tvr | · Ile | Thr | Glu | Glu | Leu | Arg | -         | Pro | Tyr | Ars | Asn | Leu | Pro |     |

|     |     | 240 |     |     |      |     | 245 |     |      |     |     | 250 |     |     |     |      |
|-----|-----|-----|-----|-----|------|-----|-----|-----|------|-----|-----|-----|-----|-----|-----|------|
| ttg | gcc | att | atc | atc | ggg  | atc | ccc | ctg | gtg  | acg | gcg | tgc | tac | atc | ctc | 996  |
| Leu | Ala | Ile | Ile | Ile | Gly  | Ile | Pro | Leu | Val  | Thr | Ala | Cys | Tyr | Ile | Leu |      |
|     | 255 |     |     |     |      | 260 |     |     |      |     | 265 |     |     |     |     |      |
| atg | aac | gtg | tcc | tac | ttc  | acc | gtg | atg | act  | gcc | acc | gaa | ctc | ctg | cag | 1044 |
| Met | Asn | Val | Ser | Tyr | Phe  | Thr | Val | Met | Thr  | Ala | Thr | Glu | Leu | Leu | Gln |      |
| 270 |     |     |     |     | 275  |     |     |     |      | 280 |     |     |     |     | 285 |      |
| tcc | cag | gcg | gtg | gct | gtg  | aca | ttt | ggt | gac  | cgt | gtt | ctc | tat | cct | gct | 1092 |
| Ser | Gln | Ala | Val | Ala | Val  | Thr | Phe | Gly | Asp  | Arg | Val | Leu | Tyr | Pro | Ala |      |
|     |     |     |     | 290 |      |     |     |     | 295  |     |     |     |     | 300 |     |      |
| tct | tgg | atc | gtt | cca | ctt  | ttt | gtg | gca | ttt  | tca | acc | atc | ggt | gct | gct | 1140 |
| Ser | Trp | Ile | Val | Pro | Leu  | Phe | Val | Ala | Phe  | Ser | Thr | Ile | Gly | Ala | Ala |      |
|     |     |     | 305 |     |      |     |     | 310 |      |     |     |     | 315 |     |     |      |
| aac | ggg | acc | tgc | ttc | aca  | gcg | ggc | aga | ctc  | att | tac | gtg | gcg | ggc | cgg | 1188 |
| Asn | Gly | Thr | Cys | Phe | Thr  | Ala | Gly | Arg | Leu  | Ile | Tyr | Val | Ala | Gly | Arg |      |
|     |     | 320 |     |     |      |     | 325 |     |      |     |     | 330 |     |     |     |      |
| gag | ggt | cac | atg | ctc | aaa. | gtg | ctt | tct | tac  | atc | agc | gtc | agg | cgc | ctc | 1236 |
| Glu | Gly | His | Met | Leu | Lys  | Val | Leu | Ser | Tyr  | Ile | Ser | Val | Arg | Arg | Leu |      |
|     | 335 |     |     |     |      | 340 |     |     |      |     | 345 |     |     |     |     |      |
| act | cca | gcc | ccc | gcc | atc  | atc | ttt | tat | ggt  | atc | ata | gca | acg | att | tat | 1284 |
| Thr | Pro | Ala | Pro | Ala | Ile  | Ile | Phe | Tyr | Gly  | Ile | Ile | Ala | Thr | Ile | Tyr |      |
| 350 |     |     |     |     | 355  |     |     |     |      | 360 |     |     |     |     | 365 |      |
| atc | atc | cct | ggt | gac | ata  | aac | tcg | tta | gtc  | aat | tat | ttc | agc | ttt | gcc | 1332 |
| Ile | Ile | Pro | Gly | Asp | Ile  | Asn | Ser | Leu | Val. | Asn | Tyr | Phe | Ser | Phe | Ala |      |
|     |     |     |     | 370 |      |     |     | ŕ   | 375  |     |     |     |     | 380 |     |      |

| gca | tgg  | ctg | ttt  | tat  | ggc  | ctg  | acg  | att  | cta  | gga  | ctc  | atc  | gtg  | atg  | aga    | 1380   |
|-----|------|-----|------|------|------|------|------|------|------|------|------|------|------|------|--------|--------|
| Ala | Trp  | Leu | Phe  | Tyr  | Gly, | Leu  | Thr  | Ile  | Leu  | Gly  | Leu  | Ile  | Val  | Met  | Arg    |        |
|     |      |     | 385  |      |      |      |      | 390  |      |      |      |      | 395  |      |        |        |
| ttt | aca  | agg | aaa  | gag  | ctg  | gaa  | agg  | cct  | atc  | aag  | gtg  | ccc  | gta  | gtc  | att    | 1428   |
| Phe | Thr  | Arg | Lys  | Glu  | Leu  | Glu  | Arg  | Pro  | Ile  | Lys  | Val  | Pro  | Val  | Val  | Ile    |        |
|     |      | 400 |      |      |      |      | 405  |      |      |      |      | 410  |      |      |        |        |
| ссс | gtc  | ttg | atg  | aca  | ctc  | atc  | tct  | gtg  | ttt  | ttg  | ġtt  | ctg  | gct  | cca  | atc    | 1476   |
| Pro | Val  | Leu | Met  | Thr  | Leu  | Ile  | Ser  | Val  | Phe  | Leu  | Val  | Leu  | Ala  | Pro  | Ile    |        |
|     | 415  |     |      |      |      | 420  |      |      |      |      | 425  |      |      |      |        |        |
| atc | agc  | aag | ccc  | acc  | tgg  | gag  | tac  | ctc  | tac  | tgt  | gtg  | ctg  | ttt  | ata  | tta    | . 1524 |
| Ile | Ser  | Lys | Pro  | Thr  | Trp  | Glu  | Tyr  | Leu  | Tyr  | Cys  | Val  | Leu  | Phe  | Ile  | Leu    |        |
| 430 |      |     |      |      | 435  |      |      |      |      | 440  |      |      |      |      | 445    |        |
| agc | ggc  | ctt | tta  | ttt  | tac  | ttc  | ctg  | ttt  | gtc  | cac  | tac  | aag  | ttt  | gga  | tgg    | 1572   |
| Ser | Gly  | Leu | Leu  | Phe  | Tyr  | Phe  | Leu  | Phe  | Val  | His  | Tyr  | Lys  | Phe  | Gly  | Trp    |        |
|     |      |     |      | 450  |      |      |      |      | 455  |      |      |      |      | 460  |        |        |
| gct | cag  | aaa | atc  | tca  | aag  | ccg  | att  | acc  | atg  | cac  | ctt  | cag  | atg  | cta  | atg    | 1620   |
| Ala | Gln  | Lys | Ile  | Ser  | Lys  | Pro  | Ile  | Thr  | Met  | His  | Leu  | Gln  | Met  | Leu  | Met    |        |
|     |      |     | 465  |      |      |      |      | 470  |      |      |      |      | 475  |      |        |        |
| gaa | gtg  | gtc | cca  | ccg  | gag  | gaa  | gac  | cct  | gag  | taa  | caag | ctc  | cgtc | tctt | gt     | 1670   |
| Glu | Val  | Val | Pro  | Pro  | Glu  | Glu  | Asp  | Pro  | Glu  |      |      |      |      |      |        |        |
|     |      | 480 |      |      |      |      | 485  |      |      |      |      |      |      |      |        |        |
| agc | caag | tca | gctg | aatt | ta t | tttc | ttaa | g ca | atat | ttgt | ggt  | tatt | tct  | tcct | tttttt | 1730   |
| ctt | acga | ata | aaat | atac | tc a | gatg | ttt  |      |      |      |      |      |      |      |        | 1758   |

| <211 | > 15  | 550   |      |       |       |       |       |          |       |       |       |       |       |       |     |     |     |
|------|-------|-------|------|-------|-------|-------|-------|----------|-------|-------|-------|-------|-------|-------|-----|-----|-----|
| <212 | :> DN | IA .  |      |       |       |       |       |          |       |       |       |       |       |       |     |     |     |
| <213 | > Hc  | omo s | apie | ens   |       |       | ٠     |          |       |       |       | •     |       |       |     |     |     |
| <220 | )>    |       |      |       |       |       |       |          |       |       |       |       |       |       |     |     |     |
| <221 | > CI  | os    |      |       |       |       |       |          |       |       |       |       |       |       |     |     |     |
| <222 | !> (1 | 154). | (1   | 281)  |       |       |       |          |       |       |       |       |       |       |     |     |     |
| <400 | )> 54 | 1     |      |       |       |       |       | ٠        |       |       |       |       |       |       |     |     |     |
| ctct | gttt  | ac c  | gaga | agago | c cg  | gtcca | agtt  | ggg      | geted | atc   | gctg  | gccc1 | tcg ( | ctcc  | cct | tcg | 60  |
| gggc | ctc   | ege o | cgcc | tggg  | ga ag | gcaga | igaga | a aag    | gccgg | gcc   | cago  | ccti  | tcc 1 | tcace | cct | tcc | 120 |
| ccto | cccg  | gca o | cgcc | cgga  | ig ag | ggtcg | gace  | g gcg    | g atg | g acc | ccc   | cag   | g cc  | c gc  | c g | ga  | 174 |
|      |       |       |      |       |       |       |       |          | Met   | t Thi | r Pro | Glr   | n Pro | o Ala | a G | ly  |     |
|      |       |       |      |       |       |       |       |          | ]     | l     |       |       | į     | 5     |     |     |     |
| ссс  | ccg   | gat   | ggg  | ggc   | tgg   | ggc   | tgg   | gtg      | gtg   | gcg   | gcc   | gca   | gcc   | ttc   | gc  | g   | 222 |
| Pro  | Pro   | Asp   | Gly  | Gly   | Trp   | Gly   | Trp   | Val      | Val   | Ala   | Ala   | Ala   | Ala   | Phe   | Al  | .a  |     |
|      |       | 10    |      |       |       |       | 15    |          |       |       |       | 20    |       |       |     |     |     |
| ata  | aac   | ggg   | ctg  | tcc   | tac   | ggg   | ctg   | ctg      | cgc   | tcg   | ctg   | ggc   | ctt   | gcc   | tt  | c   | 270 |
| Ile  | Asn   | Gly   | Leu  | Ser   | Tyr   | Gly   | Leu   | Leu      | Arg   | Ser   | Leu   | Gly   | Leu   | Ala   | Ph  | ie  |     |
|      | 25    |       |      |       |       | 30    |       |          |       |       | 35    |       |       |       |     |     |     |
| cct  | gac   | ctt   | gcc  | gag   | cac   | ttt   | gac   | cga      | agc   | gcc   | cag   | gac   | act   | gcg   | tg  | gg  | 318 |
| Pro  | Asp   | Leu   | Ala  | Glu   | His   | Phe   | Asp   | Arg      | Ser   | Ala   | Gln   | Asp   | Thr   | Ala   | Tr  | rp  |     |
| 40   |       |       |      |       | 45    |       |       |          |       | 50    |       |       |       |       | 5   | 55  |     |
| atc  | agc   | gcc   | ctg  | gcc   | ctg   | gcc   | gtg   | cag      | cag   | gca   | gcc   | agc   | ccc   | gtg   | gg  | gc  | 366 |
| Ile  | Ser   | Ala   | Leu  | Ala   | Leu   | Ala   | Val   | Gln      | Gln   | Ala   | Ala   | Ser   | Pro   | Val   | G]  | ly  |     |
|      |       |       |      | 60    |       |       |       | <i>/</i> | _65   |       |       |       |       | 70    |     |     |     |
| age  | acc   | ctø   | age  | aco   | cac   | tσσ   | σσσ   | acc      | cac   | ccc   | σtσ   | ata   | ata   | a++   | a.  | ~~  | 417 |

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| Ser | Ala | Leu | Ser | Thr | Arg | Trp              | Gly | Ala | Arg       | Pro | Val | Val | Met | Val | Gly |     |
|-----|-----|-----|-----|-----|-----|------------------|-----|-----|-----------|-----|-----|-----|-----|-----|-----|-----|
|     |     |     | 75  |     |     |                  |     | 80  |           |     |     |     | 85  |     |     |     |
| ggc | gtc | ctc | gcc | tcg | ctg | ggc              | ttc | gtc | ttc       | tcg | gct | ttc | gcc | agc | ggt | 462 |
| Gly | Val | Leụ | Ala | Ser | Leu | Gly <sup>°</sup> | Phe | Val | Phe       | Ser | Ala | Phe | Ala | Ser | Gly |     |
|     |     | 90  |     |     |     |                  | 95  |     |           |     |     | 100 |     |     |     |     |
| ctg | ctg | cat | ctc | tac | ctc | ggc              | ctg | ggc | ctc       | ctc | gct | ggc | ttt | ggt | tgg | 510 |
| Leu | Leu | His | Leu | Tyr | Leu | Gly              | Leu | Gly | Leu       | Leu | Ala | Gly | Phe | Gly | Trp |     |
|     | 105 |     |     |     |     | 110              |     |     |           |     | 115 |     |     |     |     |     |
| gcc | ctg | gtg | ttc | gcc | ccc | gcc              | cta | ggc | acc       | ctc | tcg | cgt | tac | ttc | tcc | 558 |
| Ala | Leu | Val | Phe | Ala | Pro | Ala              | Leu | Gly | Thr       | Leu | Ser | Arg | Tyr | Phe | Ser |     |
| 120 |     |     |     |     | 125 |                  |     |     |           | 130 |     |     |     |     | 135 |     |
| cgc | cgt | cga | gtc | ttg | gcg | gtg              | ggg | ctg | gcg       | ctc | acc | ggc | aac | ggg | gcc | 606 |
| Arg | Arg | Arg | Val | Leu | Ala | Val              | Gly | Leu | Ala       | Leu | Thr | Gly | Asn | Gly | Ala |     |
|     |     |     |     | 140 |     |                  |     |     | 145       |     |     |     |     | 150 |     |     |
| tcc | tcg | ctg | ctc | ctg | gcg | ccc              | gcc | ttg | cag       | ctt | ctc | ctc | gat | act | ttc | 654 |
| Ser | Ser | Leu | Leu | Leu | Ala | Pro              | Ala | Leu | Gln       | Leu | Leu | Leu | Asp | Thr | Phe |     |
|     |     |     | 155 |     |     |                  |     | 160 |           |     |     |     | 165 |     |     |     |
| ggc | tgg | cgg | ggc | gct | ctg | ctc              | ctc | ctc | ggc       | gcg | atc | acc | ctc | cac | ctc | 702 |
| Gly | Trp | Arg | Gly | Ala | Leu | Leu              | Leu | Leu | Gly       | Ala | Ile | Thr | Leu | His | Leu |     |
|     |     | 170 |     |     |     |                  | 175 |     |           |     |     | 180 |     |     |     |     |
| acc | ccc | tgt | ggc | gcc | ctg | ctg              | cta | ccc | ctg       | gtc | ctt | cct | gga | gac | ccc | 750 |
| Thr | Pro | Cys | Gly | Ala | Leu | Leu              | Leu | Pro | Leu       | Val | Leu | Pro | Gly | Asp | Pro |     |
|     | 185 |     |     |     |     | 190              |     |     |           |     | 195 |     |     | •   |     |     |
| cca | gcc | cca | ccg | cgt | agt | ccc              | cta | gct | gcc<br>سر | ctc | ggc | ctg | agt | ctg | ttc | 798 |
| Pro | Ala | Pro | Pro | Arg | Ser | Pro              | Leu | Ala | Ala       | Leu | Gly | Leu | Ser | Leu | Phe |     |

| 200 |      |     |     |     | 205 |                  |     |     |     | 210 |     |     |     |     | 215 |      |
|-----|------|-----|-----|-----|-----|------------------|-----|-----|-----|-----|-----|-----|-----|-----|-----|------|
| aca | cgc  | cgg | gcc | ttc | tca | atc <sub>.</sub> | ttt | gct | cta | ggc | aca | gcc | ctg | gtt | ggg | 846  |
| Thr | Arg  | Arg | Ala | Phe | Ser | Ile              | Phe | Ala | Leu | Gly | Thr | Ala | Leu | Val | Gly |      |
|     |      |     |     | 220 |     |                  |     |     | 225 |     |     |     |     | 230 |     |      |
| ggc | ggg  | tac | ttc | gtt | cct | tac              | gtg | cac | ttg | gct | ccc | cgc | ttt | aga | ccg | 894  |
| Gly | Gly  | Tyr | Phe | Val | Pro | Tyr              | Val | His | Leu | Ala | Pro | Arg | Phe | Arg | Pro |      |
|     |      |     | 235 |     |     |                  |     | 240 |     |     |     |     | 245 |     |     |      |
| ggg | cct  | ggg | ggg | ata | cgg | agc              | agc | gct | ggt | ggt | ggc | cgt | ggc | tgc | gat | 942  |
| Gly | Pro  | Gly | Gly | Ile | Arg | Ser              | Ser | Ala | Gly | Gly | Gly | Arg | Gly | Cys | Asp |      |
|     |      | 250 |     |     |     |                  | 255 |     |     |     |     | 260 |     |     |     |      |
| ggg | gga  | tgc | ggg | cgc | ccg | gct              | ggt | ctg | cgg | gtg | gct | ggc | aga | cca | agg | 990  |
| Gly | G1y  | Cys | Gly | Arg | Pro | Ala              | Gly | Leu | Arg | Val | Ala | Gly | Arg | Pro | Arg |      |
|     | 265  |     |     |     |     | 270              |     |     |     |     | 275 |     |     |     |     |      |
| ctg | ggt  | gcc | cct | ccc | gcg | gct              | gct | ggc | cgt | att | cgg | ggc | tct | gac | tgg | 1038 |
| Leu | Gly  | Ala | Pro | Pro | Ala | Ala              | Ala | Gly | Arg | Ile | Arg | Gly | Ser | Asp | Trp |      |
| 280 |      |     |     |     | 285 |                  |     |     |     | 290 |     |     |     |     | 295 |      |
| gct | ggg  | gct | gtg | ggt | ggt | ggg              | gct | ggt | gcc | cgt | ggt | ggg | cgg | cga | aga | 1086 |
| Ala | G1 y | Ala | Val | Gly | Gly | Gly              | Ala | Gly | Ala | Arg | Gly | Gly | Arg | Arg | Arg |      |
|     |      |     |     | 300 |     |                  |     |     | 305 |     |     |     |     | 310 |     |      |
| gag | ctg  | ggg | ggg | tcc | cct | gct              | ggc | cgc | ggc | tgt | ggc | cta | tgg | gct | gag | 1134 |
| Glu | Leu  | Gly | Gly | Ser | Pro | Ala              | Gly | Arg | Gly | Cys | Gly | Leu | Trp | Ala | Glu |      |
|     |      |     | 315 |     |     |                  | •   | 320 |     |     |     |     | 325 |     |     |      |
| cgc | ggg  | gag | tta | cgc | ccc | gct              | ggt | ttt | cgg | tgt | act | ссс | cgg | gct | ggt | 1182 |
| Arg | Gly  | Glu | Leu | Arg | Pro | Ala              | Gly | Phe | Ąrg | Cys | Thr | Pro | Arg | Ala | Gly |      |
|     |      | 330 |     |     |     |                  | 335 | /   |     |     |     | 340 |     |     |     |      |

| ggg  | cgt  | cgg   | agg  | tgt   | ggt  | gca  | ggc  | cac   | agg  | gct  | ggt | gat   | gat   | gct  | gat   | 1230   |
|------|------|-------|------|-------|------|------|------|-------|------|------|-----|-------|-------|------|-------|--------|
| Gly  | Arg  | Arg   | Arg  | Cys   | Gly  | Ala  | Gly  | His   | Arg  | Ala  | Gly | Asp   | Asp   | Ala  | Asp   |        |
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| gag  | cct  | cgg   | ggg  | gct   | cct  | ggg  | ccc  | tcc   | cct  | gtc  | agg | ctt   | cct   | aag  | gga   | 1278   |
| Glu  | Pro  | Arg   | Gly  | Ala   | Pro  | Gly  | Pro  | Ser   | Pro  | Val  | Arg | Leu   | Pro   | Lys  | Gly   |        |
| 360  |      |       |      |       | 365  |      |      |       |      | 370  |     |       |       |      | 375   |        |
| tg : | agac | agga  | ga c | ttcad | ccgc | c tc | tttc | ctcc  | tgt  | ctgg | ttc | tttga | atcc  | tc   |       | 1330   |
| tcc  | ggca | gct   | tcat | ctaca | at a | gggt | tgcc | c agg | ggcg | ctgc | cct | cctg  | tgg   | tcca | geete | c 1390 |
| cct  | ccag | cca   | cgcc | tccc  | cc a | gaga | cggg | g ga  | gctg | cttc | ccg | ctcc  | cca ; | ggca | gtctt | g 1450 |
| ctg  | tccc | cag   | gagg | ccct  | gg c | tcca | ctct | g ga  | cacc | actt | gtt | gatta | att   | ttct | tgttt | g 1510 |
| agc  | ccct | ccc ( | ccaa | taaa  | ga a | tttt | tato | g gg  | tttt | cctg |     |       |       |      |       | 1550   |
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<212> DNA

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<221> CDS

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**<400> 55** 

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Met Ala Thr Thr Ala

1 5

gcg ccg gcg ggc gcc cga aat gga gct ggc ccg gaa tgg gga ggg 163

| Ala | Pro | Ala  | Gly | Gly | Ala | Arg | Asn  | Gly | Ala | Gly | Pro | Glu | Trp | Gly | Gly   |     |
|-----|-----|------|-----|-----|-----|-----|------|-----|-----|-----|-----|-----|-----|-----|-------|-----|
|     |     |      |     | 10  |     |     |      |     | 15  |     |     |     |     | 20  |       |     |
| ttc | gaa | gaa  | aac | atc | cag | ggc | gga  | ggc | tca | gct | gtg | att | gac | atg | gag   | 211 |
| Phe | Glu | Glu  | Asn | Ile | Gln | Gly | Gly  | G1y | Ser | Ala | Val | Ile | Asp | Met | Glu   |     |
|     |     |      | 25  |     |     |     |      | 30  |     |     |     |     | 35  |     |       |     |
| aac | atg | gat  | gat | acc | tca | ggc | tct  | agc | ttc | gag | gat | atg | ggt | gag | ctg   | 259 |
| Asn | Met | Asp  | Asp | Thr | Ser | Gly | Ser  | Ser | Phe | Glu | Asp | Met | Gly | Glu | Leu   |     |
|     |     | 40   |     |     |     |     | 45   |     |     |     |     | 50  |     |     |       |     |
| cat | cag | cgc  | ctg | cgc | gag | gaa | gaa  | gta | gac | gct | gat | gca | gct | gat | gca   | 307 |
| His | Gln | Arg. | Leu | Arg | Glu | Glu | G1u  | Val | Asp | Ala | Asp | Ala | Ala | Asp | Ala   |     |
|     | 55  |      |     |     |     | 60  |      |     |     |     | 65  |     |     |     |       |     |
| gct | gct | gct  | gaa | gag | gag | gat | gga  | gag | ttc | ctg | ggc | atg | aag | ggc | ttt   | 355 |
| Ala | Ala | Ala  | Glu | Glu | Glu | Asp | Gly  | Glu | Phe | Leu | Gly | Met | Lys | Gly | Phe   |     |
| 70  |     |      |     |     | 75  |     |      |     |     | 80  |     |     |     |     | 85    |     |
| aag | gga | cag  | ctg | agc | cgg | cag | gtg  | gca | gat | cag | atg | tgg | cag | gct | ggg   | 403 |
| Lys | Gly | Gln  | Leu | Ser | Arg | Gln | Val  | Ala | Asp | Gln | Met | Trp | G1n | Ala | Gly   |     |
|     |     |      |     | 90  |     |     |      |     | 95  |     |     |     |     | 100 |       |     |
| aaa | aga | caa  | gcc | tcc | agg | gcc | ttc  | agc | ttg | tac | gcc | aac | atc | gac | atc   | 451 |
| Lys | Arg | Gln  | Ala | Ser | Arg | Ala | Phe  | Ser | Leu | Tyr | Ala | Asn | Ile | Asp | Ile   |     |
|     |     |      | 105 |     |     |     |      | 110 |     |     |     |     | 115 |     |       |     |
| ctc | aga | ccc  | tac | ttt | gat | gtg | gag  | cct | gct | cag | gtg | cga | agc | agg | ctc   | 499 |
| Leu | Arg | Pro  | Tyr | Phe | Asp | Val | Glu  | Pro | Ala | Gln | Val | Arg | Ser | Arg | Leu   |     |
|     |     | 120  |     | •   |     |     | 125  |     |     |     |     | 130 |     |     |       |     |
| ctg | gag | tcc  | atg | atc | cct | atc | aag  | atg | gtc | aac | ttc | ccc | cag | aaa | att   | 547 |
| Leu | Glu | Ser  | Met | Τle | Pro | Πρ  | ī.ve | Met | Va1 | Asn | Pho | Pro | Gln | Ive | م T ا |     |

|     | 135 |     |       |     |     | 140 |     |     |            |     | 145 |     |     |     |     |     |
|-----|-----|-----|-------|-----|-----|-----|-----|-----|------------|-----|-----|-----|-----|-----|-----|-----|
| gca | ggt | gaa | ctc   | tat | gga | cct | ctc | atg | ctg        | gtc | ttc | act | ctg | gtt | gct | 595 |
| Ala | Gly | Glu | Leu   | Tyr | Gly | Pro | Leu | Met | Leu        | Val | Phe | Thr | Leu | Val | Ala |     |
| 150 |     |     |       |     | 155 |     |     |     |            | 160 |     |     |     |     | 165 |     |
| atc | cta | ctc | cat   | ggg | atg | aag | acg | tct | gac        | act | att | atc | cgg | gag | ggc | 643 |
| Ile | Leu | Leu | His   | Gly | Met | Lys | Thr | Ser | Asp        | Thr | Ile | Ile | Arg | Glu | Gly |     |
|     |     |     |       | 170 |     |     |     |     | 175        |     |     |     |     | 180 |     |     |
| acc | ctg | atg | ggc   | aca | gcc | att | ggc | acc | tgc        | ttc | ggc | tac | tgg | ctg | gga | 691 |
| Thr | Leu | Met | Gly   | Thr | Ala | Ile | Gly | Thr | Cys        | Phe | Gly | Tyr | Trp | Leu | Gly |     |
|     |     |     | 185   |     |     |     |     | 190 |            |     |     |     | 195 |     |     |     |
| gtc | tca | tcc | ttc   | att | tac | ttc | ctt | gcc | tac        | ctg | tgc | aac | gcc | cag | atc | 739 |
| Val | Ser | Ser | Phe   | Ile | Tyr | Phe | Leu | Ala | Tyr        | Leu | Cys | Asn | Ala | Gln | Ile |     |
|     |     | 200 |       |     |     |     | 205 |     |            |     |     | 210 |     |     |     |     |
| acc | atg | ctg | cag   | atg | ttg | gca | ctg | ctg | ggc        | tat | ggc | ctc | ttt | ggg | cat | 787 |
| Thr | Met | Leu | Gln   | Met | Leu | Ala | Leu | Leu | Gly        | Tyr | Gly | Leu | Phe | Gly | His |     |
|     | 215 |     |       |     |     | 220 |     |     |            |     | 225 |     |     |     |     |     |
| tgc | att | gtc | ctg   | ttc | atc | acc | tat | aat | atc        | cac | ctc | cac | gcc | ctc | ttc | 835 |
| Cys | Ile | Val | Leu   | Phe | Ile | Thr | Tyr | Asn | Ile        | His | Leu | His | Ala | Leu | Phe |     |
| 230 |     | ÷   |       |     | 235 |     |     |     |            | 240 |     |     |     |     | 245 |     |
| tac | ctc | ttc | tgg   | ctg | ttg | gtg | ggt | gga | ctg        | tcc | aca | ctg | cgc | atg | gta | 883 |
| Tyr | Leu | Phe | Trp   | Leu | Leu | Val | Gly | Gly | Leu        | Ser | Thr | Leu | Arg | Met | Val |     |
|     |     |     |       | 250 | 1   |     |     |     | 255        |     |     |     |     | 260 |     |     |
| gca | gtg | ttg | gtg   | tct | cgg | acc | gtg | ggc | ccc        | aca | cag | cgg | cte | ctc | ctc | 931 |
| Ala | Val | Leu | ı Val | Ser | Arg | Thr | Val | Gly | Pro<br>نتر | Thr | Gln | Arg | Leu | Leu | Leu |     |
|     |     |     | 265   | ,   |     |     |     | 270 | )          |     |     |     | 275 | 5   |     |     |

| tgt  | ggc   | acc   | ctg   | gct   | gcc   | cta   | cac   | atg   | ctc   | ttc  | ctg   | ctc   | tat   | ctg   | cat    | 979  |
|------|-------|-------|-------|-------|-------|-------|-------|-------|-------|------|-------|-------|-------|-------|--------|------|
| Cys  | Gly   | Thr   | Leu   | Ala   | Ala   | Leu   | His   | Meţ   | Leu   | Phe  | Leu   | Leu   | Tyr   | Leu   | His    |      |
|      |       | 280   |       |       |       |       | 285   |       |       |      |       | 290   |       |       |        | ÷    |
| ttt  | gcc   | tac   | cac   | aaa   | gtg   | gta   | gag   | ggg   | atc   | ctg  | gac   | aca   | ctg   | gag   | ggc    | 1027 |
| Phe  | Ala   | Tyr   | His   | Lys   | Val   | Val   | Glu   | Gly   | Ile   | Leu  | Asp   | Thr   | Leu   | G1u   | Gly    |      |
|      | 295   |       |       |       |       | 300   |       |       |       |      | 305   |       |       |       |        |      |
| ccc  | aac   | atc   | ccg   | ccc   | atc   | cag   | agg   | gtc   | ссс   | aga  | gac   | atc   | cct   | gcc   | atg    | 1075 |
| Pro  | Asn   | Ile   | Pro   | Pro   | Ile   | Gln   | Arg   | Val   | Pro   | Arg  | Asp   | Ile   | Pro   | Ala   | Met    |      |
| 310  |       |       |       |       | 315   |       |       |       |       | 320  |       |       |       |       | 325    |      |
| ctc  | cct   | gct   | gct   | cgg   | ctt   | ccc   | acc   | acc   | gtc   | ctc  | aac   | gcc   | aca   | gcc   | aaa    | 1123 |
| Leu  | Pro   | Ala   | Ala   | Arg   | Leu   | Pro   | Thr   | Thr   | Val   | Leu  | Asn   | Ala   | Thr   | Ala   | Lys    |      |
|      |       |       |       | 330   |       |       |       |       | 335   |      |       |       |       | 340   |        |      |
| gct  | gtt   | gcg   | gtg   | acc   | ctg   | cag   | tca   | cac   | tgad  | ccca | acc t | gaaa  | atte  | tt    |        | 1170 |
| Ala  | Val   | Ala   | Val   | Thr   | Leu   | G1n   | Ser   | His   |       |      |       |       |       |       |        |      |
|      |       |       | 345   |       |       |       |       | 350   |       |      |       |       |       |       |        |      |
| ggc  | cagto | cct o | cttt  | cccg  | ca go | etgea | agaga | a gga | aggaa | agac | tatt  | aaag  | gga ( | cagto | ctgat  | 1230 |
| gaca | atgti | ttc į | gtaga | atggg | gg ti | ttgca | agct  | g cca | actga | agct | gtag  | gctgo | egt a | aagta | acctcc | 1290 |
| ttga | atgc  | ctg   | tcgg  | cacti | tc ta | gaaag | ggca  | c aag | ggcca | aaga | acto  | ectg  | gcc a | agga  | ctgcaa | 1350 |
| ggc1 | ctg   | cag ( | ccaat | tgca  | ga aa | aatgg | ggtca | a gct | tcct1 | ttga | gaad  | ccci  | tcc ( | ccac  | ctaccc | 1410 |
| ctt  | ctte  | cct ( | cttta | atct  | ct c  | caca  | attg  | t-ct1 | tgcta | aaat | atag  | gact  | tgg 1 | taati | taaaat | 1470 |
| gtt  | gattı | gaa ( | gtct  | g     |       |       |       |       |       |      |       |       |       |       | -      | 1485 |

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⟨211⟩ 2694

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| <213 | > Ho | no s | apie  | ns   |      |      |      |     |           |     |      |      |      |       |        |      |
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| gcag | gaga | ag g | gcca  | gaga | atg  | tcg  | tcc  | cag | cca       | gca | ggg  | aac  | cag  | g acc | tcc    | 112  |
|      |      |      |       |      | Met  | Ser  | Ser  | Gln | Pro       | Ala | Gly  | Asr  | Glr  | Thr   | Ser    |      |
|      |      |      |       |      | 1    |      |      |     | 5         | 5   |      |      |      | 10    | )      |      |
| ccc  | ggg  | gcc  | aca   | gag  | gac  | tac  | tcc  | tat | ggc       | agc | tgg  | tac  | atc  | gat   | gag    | 160  |
| Pro  | G1y  | Ala  | Thr   | Glu  | Asp  | Tyr  | Ser  | Tyr | Gly       | Ser | Trp  | Tyr  | Ile  | Asp   | Glu    |      |
|      |      |      | 15    |      |      |      |      | 20  |           |     |      |      | 25   | •     |        |      |
| ссс  | cag  | ggg  | ggc   | gag  | gag  | ctc  | cag  | cca | gag       | ggg | gaa  | gtg  | ссс  | tcc   | tgc    | 208  |
| Pro  | Gln  | Gly  | Gly   | Glu  | Glu  | Leu  | Gln  | Pro | Glu       | Gly | Glu  | Val  | Pro  | Ser   | Cys    |      |
|      |      | 30   |       |      |      |      | 35   |     |           |     |      | 40   |      |       |        |      |
| cac  | acc  | agc  | ata   | cca  | ccc  | ggc  | ctg  | tac | cac       | gcc | tgc  | ctg  | gcc  | tcg   | ctg    | 256  |
| His  | Thr  | Ser  | Ile   | Pro  | Pro  | Gly  | Leu  | Tyr | His       | Ala | Cys  | Leu  | Ala  | Ser   | Leu    |      |
|      | 45   |      |       |      |      | 50   |      |     |           |     | 55   |      |      |       |        |      |
| tca  | atc  | ctt  | gtg   | ctg  | ctg  | ctc  | ctg  | gcc | atg       | ctg | gtg  | agg  | cgc  | cgc   | cag    | 304  |
| Ser  | Ile  | Leu  | Val   | Leu  | Leu  | Leu  | Leu  | Ala | Met       | Leu | Val  | Arg  | Arg  | Arg   | Gln    |      |
| 60   |      |      |       |      | 65   |      |      |     |           | 70  |      |      |      |       | 75     |      |
| ctc  | tgg  | cct  | gac   | tgt  | gtg  | cgt  | ggc  | agg | ccc       | ggc | ctg  | ccc  | agc  | cct   | gtg    | 352  |
| Leu  | Trp  | Pro  | Asp   | Cys  | Val  | Arg  | Gly  | Arg | Pro       | Gly | Leu  | Pro  | Ser  | Pro   | Val    |      |
|      |      |      |       | 80   |      |      |      |     | 85        |     |      |      |      | 90    |        |      |
| gat  | ttc  | ttg  | gct   | ggg  | gac  | agg  | ccc  | cgg | ين<br>gca | gtg | cct  | gct  | gct  | gtt   | ttc    | 400  |

| Asp | Phe | Leu | Ala | Gly | Asp | Arg | Pro | Arg | Ala | Val | Pro | Ala | Ala | Val | Phe |     |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
|     |     |     | 95  |     |     |     |     | 100 |     |     |     |     | 105 |     |     |     |
| atg | gtc | ċtc | ttg | agc | tcc | ctg | tgt | ttg | ctg | ctc | ccc | gac | gag | gac | gca | 448 |
| Met | Val | Leu | Leu | Ser | Ser | Leu | Cys | Leu | Leu | Leu | Pro | Asp | Glu | Asp | Ala |     |
|     |     | 110 |     |     |     |     | 115 |     |     |     |     | 120 |     |     |     |     |
| ttg | ccc | ttc | ctg | act | ctc | gcc | tca | gca | ccc | agc | caa | gat | ggg | aaa | act | 496 |
| Leu | Pro | Phe | Leu | Thr | Leu | Ala | Ser | Ala | Pro | Ser | Gln | Asp | Gly | Lys | Thr |     |
|     | 125 |     |     |     |     | 130 |     |     |     |     | 135 |     |     |     |     |     |
| gag | gct | cca | aga | ggg | gcc | tgg | aag | ata | ctg | gga | ctg | ttc | tat | tat | gct | 544 |
| Glu | Ala | Pro | Arg | Gly | Ala | Trp | Lys | Ile | Leu | Gly | Leu | Phe | Tyr | Tyr | Ala |     |
| 140 |     |     |     |     | 145 |     |     |     |     | 150 |     |     |     |     | 155 |     |
| gcc | ctc | tac | tac | cct | ctg | gct | gcc | tgt | gcc | acg | gct | ggc | cac | aca | gct | 592 |
| Ala | Leu | Tyr | Tyr | Pro | Leu | Ala | Ala | Cys | Ala | Thr | Ala | Gly | His | Thr | Ala |     |
|     |     |     |     | 160 |     |     |     |     | 165 |     |     |     |     | 170 |     |     |
| gca | cac | ctg | ctc | ggc | agc | acg | ctg | tcc | tgg | gcc | cac | ctt | ggg | gtc | cag | 640 |
| Ala | His | Leu | Leu | Gly | Ser | Thr | Leu | Ser | Trp | Ala | His | Leu | Gly | Val | Gln |     |
|     |     |     | 175 |     |     |     |     | 180 |     |     |     |     | 185 |     |     |     |
| gtc | tgg | cag | agg | gca | gag | tgt | ccc | cag | gtg | ccc | aag | atc | tac | aag | tac | 688 |
| Val | Trp | Gln | Arg | Ala | Glu | Cys | Pro | G1n | Val | Pro | Lys | Ile | Tyr | Lys | Tyr |     |
|     |     | 190 |     |     |     |     | 195 |     |     |     |     | 200 |     |     |     |     |
| tac | tcc | ctg | ctg | gcc | tcc | ctg | cct | ctc | ctg | ctg | ggc | ctc | gga | ttc | ctg | 736 |
| Tyr | Ser | Leu | Leu | Ala | Ser | Leu | Pro | Leu | Leu | Leu | Gly | Leu | Gly | Phe | Leu |     |
|     | 205 |     |     |     |     | 210 |     |     |     |     | 215 |     |     |     |     |     |
| agc | ctt | tgg | tac | cct | gtg | cag | ctg | gtg | aga | agc | ttc | agc | cgt | agg | aca | 784 |
| Ser | Leu | Trn | Tvr | Pro | Val | Gln | Len | Val | Aro | Ser | Phe | Ser | Ara | Ara | Thr | •   |

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| 220 |     |     |     |     | 225 |     |     |     |     | 230 |     |     |     |     | 235 |      |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|------|
| gga | gca | ggc | tcc | aag | ggg | ctg | cag | agc | agc | tac | tct | gag | gaa | tat | ctg | 832  |
| Gly | Ala | Gly | Ser | Lys | Gly | Leu | Gln | Ser | Ser | Tyr | Ser | Glu | Glu | Tyr | Leu |      |
|     |     |     |     | 240 |     |     |     |     | 245 |     |     |     |     | 250 |     |      |
| agg | aac | ctc | ctt | tgc | agg | aag | aag | ctg | gga | agc | agc | tac | cac | acc | tcc | 880  |
| Arg | Asn | Leu | Leu | Cys | Arg | Lys | Lys | Leu | Gly | Ser | Ser | Tyr | His | Thr | Ser |      |
|     |     |     | 255 |     |     |     |     | 260 |     |     |     |     | 265 |     |     |      |
| aag | cat | ggc | ttc | ctg | tcc | tgg | gcc | cgc | gtc | tgc | ttg | aga | cac | tgc | atc | 928  |
| Lys | His | Gly | Phe | Leu | Ser | Trp | Ala | Arg | Val | Cys | Leu | Arg | His | Cys | Ile |      |
|     |     | 270 |     |     |     |     | 275 |     |     |     |     | 280 |     |     |     |      |
| tac | act | cca | cag | cca | gga | ttc | cat | ctc | ccg | ctg | aag | ctg | gtg | ctt | tca | 976  |
| Tyr | Thr | Pro | Gln | Pro | Gly | Phe | His | Leu | Pro | Leu | Lys | Leu | Val | Leu | Ser |      |
|     | 285 |     |     |     |     | 290 |     |     |     |     | 295 |     |     |     |     |      |
| gct | aca | ctg | aca | ggg | acg | gcc | att | tac | cag | gtg | gcc | ctg | ctg | ctg | ctg | 1024 |
| Ala | Thr | Leu | Thr | Gly | Thr | Ala | Ile | Tyr | Gln | Val | Ala | Leu | Leu | Leu | Leu |      |
| 300 |     |     |     |     | 305 |     |     |     |     | 310 |     |     |     |     | 315 |      |
| gtg | ggc | gtg | gta | ccc | act | atc | cag | aag | gtg | agg | gca | ggg | gtc | acc | acg | 1072 |
| Val | Gly | Val | Val | Pro | Thr | Ile | Gln | Lys | Val | Arg | Ala | Gly | Val | Thr | Thr |      |
|     |     |     |     | 320 |     |     |     |     | 325 |     |     |     |     | 330 |     |      |
| gat | gtc | tcc | tac | ctg | ctg | gcc | ggc | ttt | gga | atc | gtg | ctc | tcc | gag | gac | 1120 |
| Asp | Val | Ser | Tyr | Leu | Leu | Ala | Gly | Phe | Gly | Ile | Val | Leu | Ser | Glu | Asp |      |
|     |     |     | 335 |     |     |     |     | 340 |     |     |     |     | 345 |     |     |      |
| aag | cag | gag | gtg | gtg | gag | ctg | gtg | aag | cac | cat | ctg | tgg | gct | ctg | gaa | 1168 |
| Lys | Gln | Glu | Val | Val | Glu | Leu | Val | Lys | His | His | Leu | Trp | Ala | Leu | Glu |      |
|     |     | 350 | )   |     |     |     | 355 |     | سرر |     |     | 360 | )   |     |     |      |

| gtg | tgc | tac | atc | tca | gcc | ttg | gtc | ttg   | tcc         | tgc | tta        | ctc | acc | ttc | ctg | 1216 |
|-----|-----|-----|-----|-----|-----|-----|-----|-------|-------------|-----|------------|-----|-----|-----|-----|------|
| Val | Cys | Tyr | Ile | Ser | Ala | Leu | Val | Leu   | Ser         | Cys | Leu        | Leu | Thr | Phe | Leu |      |
|     | 365 |     | ,   |     |     | 370 |     |       |             |     | 375        |     | ٠   |     | •   |      |
| gtc | ctg | atg | cgc | tca | ctg | gtg | aca | cac   | agg         | acc | aac        | ctt | cga | gct | ctg | 1264 |
| Val | Leu | Met | Arg | Ser | Leu | Val | Thr | His   | Arg         | Thr | Asn        | Leu | Arg | Ala | Leu |      |
| 380 |     |     |     |     | 385 |     |     |       |             | 390 |            |     |     |     | 395 |      |
| cac | cga | gga | gct | gcc | ctg | gac | ttg | agt   | ссс         | ttg | cat        | cgg | agt | ccc | cat | 1312 |
| His | Arg | Gly | Ala | Ala | Leu | Asp | Leu | Ser   | Pro         | Leu | His        | Arg | Ser | Pro | His |      |
|     |     |     |     | 400 |     |     |     |       | 405         |     |            |     |     | 410 |     |      |
| ссс | tcc | cgc | caa | gcc | ata | ttc | tgt | tgg   | atg         | agc | ttc        | agt | gcc | tac | cag | 1360 |
| Pro | Ser | Arg | Gln | Ala | Ile | Phe | Cys | Trp   | Met         | Ser | Phe        | Ser | Ala | Tyr | Gln |      |
|     |     |     | 415 |     |     |     |     | 420   |             |     |            |     | 425 |     |     |      |
| aca | gcc | ttt | atc | tgc | ctt | ggg | ctc | ctg   | gtg         | cag | cag        | atc | atc | ttc | ttc | 1408 |
| Thr | Ala | Phe | Ile | Cys | Leu | Gly | Leu | Leu   | Val         | Gln | Gln        | Ile | Ile | Phe | Phe |      |
|     |     | 430 |     |     |     |     | 435 |       |             |     |            | 440 |     |     |     |      |
| ctg | gga | acc | acg | gcc | ctg | gcc | ttc | ctg   | gtg         | ctc | atg        | cct | gtg | ctc | cat | 1456 |
| Leu | Gly | Thr | Thr | Ala | Leu | Ala | Phe | Leu   | Val         | Leu | Met        | Pro | Val | Leu | His |      |
|     | 445 |     |     |     |     | 450 |     |       |             |     | 455        |     |     |     |     |      |
| ggc | agg | aac | ctc | ctg | ctc | ttc | cgt | tcc   | ctg         | gag | tcc        | tcg | tgg | ссс | ttc | 1504 |
| Gly | Arg | Asn | Leu | Leu | Leu | Phe | Arg | Ser   | Leu         | Glu | Ser        | Ser | Trp | Pro | Phe |      |
| 460 |     |     |     |     | 465 |     |     |       |             | 470 |            | ٠   |     |     | 475 |      |
| tgg | ctg | act | ttg | gcc | ctg | gct | gtg | atc   | ctg         | cag | aac        | atg | gca | gcc | cat | 1552 |
| Trp | Leu | Thr | Leu | Ala | Leu | Ala | Val | Ile   | Leu         | Gln | Asn        | Met | Ala | Ala | His |      |
|     |     |     |     | 480 |     |     |     |       | <u>4</u> 85 |     |            |     |     | 490 |     |      |
| too | σtc | tto | ctø | ġασ | act | cat | gat | 7 7 7 | cac         | 009 | <b>^20</b> | cto | 200 | 220 |     | 1600 |

| Trp | Val | Phe | Leu | Glu | Thr | His | Asp | Gly | His | Pro | Gln | Leu | Thr | Asn | Arg   |      |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-------|------|
|     |     |     | 495 |     |     |     |     | 500 |     |     |     |     | 505 |     |       |      |
| cga | gtg | ctc | tat | gca | gcc | acc | ttt | ctt | ctc | ttc | ccc | ctc | aat | gtg | ctg . | 1648 |
| Arg | Val | Leu | Tyr | Ala | Ala | Thr | Phe | Leu | Leu | Phe | Pro | Leu | Asn | Val | Leu   |      |
|     |     | 510 |     |     |     |     | 515 |     |     |     |     | 520 |     |     |       |      |
| gtg | ggt | gcc | atg | gtg | gcc | acc | tgg | cga | gtg | ctc | ctc | tct | gcc | ctc | tac   | 1696 |
| Val | Gly | Ala | Met | Val | Ala | Thr | Trp | Arg | Val | Leu | Leu | Ser | Ala | Leu | Tyr   |      |
|     | 525 |     |     |     |     | 530 |     |     |     |     | 535 |     |     |     |       |      |
| aac | gcc | atc | cac | ctt | ggc | cag | atg | gac | ctc | agc | ctg | ctg | cca | ccg | aga   | 1744 |
| Asn | Ala | Ile | His | Leu | Gly | Gln | Met | Asp | Leu | Ser | Leu | Leu | Pro | Pro | Arg   |      |
| 540 |     |     |     |     | 545 |     |     |     |     | 550 |     |     |     |     | 555   |      |
| gcc | gcc | act | ctc | gac | ccc | ggc | tac | tac | acg | tac | cga | aac | ttc | ttg | aag   | 1792 |
| Ala | Ala | Thr | Leu | Asp | Pro | Gly | Tyr | Tyr | Thr | Tyr | Arg | Asn | Phe | Leu | Lys   |      |
|     |     |     |     | 560 |     |     |     |     | 565 |     |     |     |     | 570 |       |      |
| att | gaa | gtc | agc | cag | tcg | cat | cca | gcc | atg | aca | gcc | ttc | tgc | tcc | ctg   | 1840 |
| Ile | Glu | Val | Ser | Gln | Ser | His | Pro | Ala | Met | Thr | Ala | Phe | Cys | Ser | Leu   |      |
|     |     |     | 575 |     |     |     |     | 580 |     |     |     |     | 585 |     |       |      |
| ctc | ctg | caa | gcg | cag | agc | ctc | cta | ccc | agg | acc | atg | gca | gcc | ccc | cag   | 1888 |
| Leu | Leu | Gln | Ala | Gln | Ser | Leu | Leu | Pro | Arg | Thr | Met | Ala | Ala | Pro | Gln   |      |
|     |     | 590 |     |     |     |     | 595 |     |     |     |     | 600 |     |     |       |      |
| gac | agc | ctc | aga | cca | ggg | gag | gaa | gac | gaa | ggg | atg | cag | ctg | cta | cag   | 1936 |
| Asp | Ser | Leu | Arg | Pro | Gly | Glu | Glu | Asp | Glu | Gly | Met | Gln | Leu | Leu | G1n   |      |
|     | 605 |     |     |     |     | 610 |     |     |     |     | 615 |     |     |     |       |      |
| aca | aag | gac | tcc | atg | gcc | aag | gga | gct | agg | ccc | ggg | gcc | agc | cgc | ggc   | 1984 |
| Thr | Lys | Asp | Ser | Met | Ala | Lys | Gly | Ala | Arg | Pro | Gly | Ala | Ser | Arg | Gly   |      |

| 620                   | 625               | 630                 | 635             |
|-----------------------|-------------------|---------------------|-----------------|
| agg gct cgc tgg ggt   | ctg gcc tac acg c | tg ctg cac aac cca  | acc ctg 2032    |
| Arg Ala Arg Trp Gly I | Leu Ala Tyr Thr L | eu Leu His Asn Pro  | Thr Leu         |
| 640                   | 6                 | 345                 | 650             |
| cag gtc ttc cgc aag a | acg gcc ctg ttg g | gt gcc aat ggt gcc  | cag ccc 2080    |
| Gln Val Phe Arg Lys   | Thr Ala Leu Leu G | Gly Ala Asn Gly Ala | Gln Pro         |
| 655                   | 660               | 665                 |                 |
| tgagggcagg gaaggtca   | ac ccacctgccc atc | tgtgctg aggcatgtto  | 2130            |
| ctgcctacca tcctcctcc  | c tecceggete tect | cccagc atcacaccag   | ccatgcagcc 2190 |
| agcaggtcct ccggatcac  | c gtggttgggt ggag | gtctgt ctgcactggg   | agcctcagga 2250 |
| gggctctgct ccacccact  | t ggctatggga gagc | cagcag gggttctgga   | gaaagaaact 2310 |
| ggtgggttag ggccttggt  | c caggagccag ttga | gccagg gcagccacat   | ccaggegtet 2370 |
| ccctaccctg gctctgcca  | t cagccttgaa gggc | ectegat gaageettet  | ctggaaccac 2430 |
| tccagcccag ctccacctc  | a goottggoot toac | gctgtg gaagcagcca   | aggcacttcc 2490 |
| tcacccctc agcgccacg   | g acctctctgg ggag | tggccg gaaagctccc   | gggcctctgg 2550 |
| cctgcagggc agcccaagte | c atgactcaga ccag | gtccca cactgagctg   | cccacactcg 2610 |
| agagccagat attttgta   | g tttttatgcc tttg | gctatt atgaaagagg   | ttagtgtgtt 2670 |
| ccctgcaata aacttgttc  | c tgag            |                     | 2694            |

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#### 122/307

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| .400. | / 51 |            |      |      |      |      |       |     |             |               |      |       |       |       |       |      |
|-------|------|------------|------|------|------|------|-------|-----|-------------|---------------|------|-------|-------|-------|-------|------|
| gggg  | tctg | ta c       | tctg | tgaa | g to | aact | gggt  | tag | tgtg        | ctc           | tctg | gatgo | ct g  | ggaat | tccag | g 60 |
| tccc  | cacc | ca g       | aaac | ccgc | a go | ate  | att   | gto | tgo         | . <b>ct</b> c | ctt  | tto   | ate   | g atg | g att | 112  |
|       |      |            |      |      |      | Met  | : Ile | Val | . Cys       | Leu           | Leu  | ı Phe | e Met | t Met | t Ile |      |
|       |      |            |      |      |      | 1    |       |     |             | 5             | •    |       |       |       | 10    |      |
| tta   | ttg  | gca        | aag  | gaa  | gtt  | caa  | ctg   | gta | gac         | caa           | aca  | gat   | tca   | cct   | tta   | 160  |
| Leu   | Leu  | Ala        | Lys  | Glu  | Val  | Gln  | Leu   | Val | Asp         | Gln           | Thr  | Asp   | Ser   | Pro   | Leu   |      |
|       |      |            |      | 15   |      |      |       |     | 20          |               |      |       |       | 25    |       |      |
| ctt   | agt  | ctc        | ctt  | gga  | cag  | aca  | agc   | tca | ctt         | tca           | tgg  | cat   | ctt   | gtg   | gat   | 208  |
| Leu   | Ser  | Leu        | Leu  | Gly  | Gln  | Thr  | Ser   | Ser | Leu         | Ser           | Trp  | His   | Leu   | Val   | Asp   |      |
|       |      |            | 30   |      |      |      |       | 35  |             |               |      |       | 40    |       |       |      |
| att   | gtg  | tcg        | tac  | cag  | agt  | gtg  | cta   | agt | tat         | ttc           | agc  | agc   | cat   | tac   | ccg   | 256  |
| Ile   | Val  | Ser        | Tyr  | Gln  | Ser  | Val  | Leu   | Ser | Tyr         | Phe           | Ser  | Ser   | His   | Tyr   | Pro   |      |
|       |      | <b>4</b> 5 |      |      |      |      | 50    |     |             |               |      | 55    |       |       |       |      |
| ccg   | tcc  | atc        | atc  | ctg  | gca  | aaa  | gaa   | tct | tat         | gct           | gaa  | tta   | atc   | atg   | aag   | 304  |
| Pro   | Ser  | Ile        | Ile  | Leu  | Ala  | Lys  | Glu   | Ser | Tyr         | Ala           | Glu  | Leu   | Ile   | Met   | Lys   |      |
|       | 60   |            |      |      |      | 65   |       |     |             |               | 70   |       |       |       |       |      |
| ctc   | cta  | aaa        | gtg  | tct  | gcg  | ggc  | ctt   | tct | att         | cct           | act  | gac   | agc   | cag   | aag   | 352  |
| Leu   | Leu  | Lys        | Val  | Ser  | Ala  | Gly  | Leu   | Ser | Ile         | Pro           | Thr  | Asp   | Ser   | Gln   | Lys   |      |
| 75    |      |            |      |      | 80   |      |       |     |             | 85            |      |       |       |       | 90    |      |
| cat   | ctt  | gat        | gca  | gtt  | cca  | aaa  | tgc   | caa | gct         | ttt           | act  | cat   | cag   | atg   | gtt   | 400  |
| His   | Leu  | Asp        | Ala  | Val  | Pro  | Lys  | Cys   | G1n | Ala         | Phe           | Thr  | His   | Gln   | Met   | . Val |      |
|       |      |            |      | 95   | ,    |      |       |     | 100         | )             |      |       |       | 105   | 5     |      |
| caa   | ttc  | ctc        | ago  | acc  | ctg  | gaa  | caa   | aat | نني<br>gga: | aaa           | ato  | acc   | tta   | a gca | a gtc | 448  |

| Gln | Phe | Leu | Ser | Thr  | Leu | Glu | Gln | Asn | Gly | Lys | Ile | Thr         | Leu | Ala | Val              |     |
|-----|-----|-----|-----|------|-----|-----|-----|-----|-----|-----|-----|-------------|-----|-----|------------------|-----|
|     |     |     | 110 |      |     |     |     | 115 |     |     |     |             | 120 |     |                  |     |
| cta | gaa | cag | gaa | atg  | tct | aag | ctc | tta | gac | gat | atc | att         | gtc | ttt | aac              | 496 |
| Leu | Glu | Gln | Glu | Met  | Ser | Lys | Leu | Leu | Asp | Asp | Ile | Ile         | Val | Phe | Asn              |     |
|     |     | 125 |     |      |     |     | 130 |     |     |     |     | 135         |     |     |                  |     |
| ccg | ссс | gac | atg | gac  | agc | cag | acc | cgc | cac | atg | gcc | ctc         | agc | agc | ctc              | 544 |
| Pro | Pro | Asp | Met | Asp  | Ser | Gln | Thr | Arg | His | Met | Ala | Leu         | Ser | Ser | Leu              |     |
|     | 140 |     |     |      |     | 145 |     |     |     |     | 150 |             |     |     |                  |     |
| ttt | atg | gaa | gtc | ctg  | atg | atg | atg | aac | aac | gcg | act | att         | cca | aca | gca              | 592 |
| Phe | Met | G1u | Val | Leu  | Met | Met | Met | Asn | Asn | Ala | Thr | Ile         | Pro | Thr | Ala              |     |
| 155 |     |     |     |      | 160 |     | •   |     |     | 165 |     |             |     |     | 170              |     |
| gag | ttc | ctt | cgg | ggc  | agt | atc | cgg | acc | tgg | att | ggc | caa         | aaa | atg | cat              | 640 |
| Glu | Phe | Leu | Arg | Gly  | Ser | Ile | Arg | Thr | Trp | Ile | Gly | Gln         | Lys | Met | His              |     |
|     |     |     |     | 175  |     |     |     |     | 180 |     |     |             |     | 185 |                  |     |
| ggg | ctg | gtg | gtg | ctg  | ccc | ctt | tta | aca | gca | gcc | tgc | cag         | agc | ctg | gcg              | 688 |
| Gly | Leu | Val | Val | Leu  | Pro | Leu | Leu | Thr | Ala | Ala | Cys | Gln         | Ser | Leu | Ala              |     |
|     |     | -   | 190 |      |     |     |     | 195 |     |     |     |             | 200 |     |                  |     |
| tcc | gtc | cgc | cac | atg  | gct | gag | act | aca | gaa | gcc | tgc | atc         | act | gcc | tac              | 736 |
| Ser | Val | Arg | His | Met  | Ala | Glu | Thr | Thr | Glu | Ala | Cys | Ile         | Thr | Ala | Tyr              |     |
|     |     | 205 |     |      |     |     | 210 |     |     |     |     | 215         |     |     |                  |     |
| ttc | aaa | gaa | agc | cct  | ctc | aat | cag | aat | tca | gga | tgg | gga         | ccc | att | ctg              | 784 |
| Phe | Lys | Glu | Ser | Pro  | Leu | Asn | Gln | Asn | Ser | Gly | Trp | Gly         | Pro | Ile | Leu              |     |
|     | 220 |     |     |      |     | 225 |     |     |     |     | 230 |             |     |     |                  |     |
| gta | tcc | ctt | cag | gtt  | ссс | gag | ctc | acc | ątg | gaa | gag | <b>t</b> tc | ctg | cag | gag              | 832 |
| Val | Ser | Len | Gln | Va 1 | Pro | Glu | Len | Thr | Ma+ | Glu | Gli | Dha         | Lou | C1r | C1 <sub>11</sub> |     |

| 235 |       |       |       |       | 240   |       |       |     |     | 245   |       |       |       |       | 250   |      |
|-----|-------|-------|-------|-------|-------|-------|-------|-----|-----|-------|-------|-------|-------|-------|-------|------|
| tgc | ctc   | acc   | ttg   | ggc   | agt   | tac   | ttg   | act | ctt | tac   | gtc   | tac   | ttg   | ctt   | cag   | 880  |
| Cys | Leu   | Thr   | Leu   | Gly   | Ser   | Tyr   | Leu   | Thr | Leu | Tyr   | Val   | Tyr   | Leu   | Leu   | Gln   |      |
|     |       |       |       | 255   |       |       |       |     | 260 |       |       |       |       | 265   |       |      |
| tgt | tta   | aac   | agc   | gaa   | cag   | act   | tta   | agg | aat | gaa   | atg   | aaa   | gtg   | ctg   | ctc   | 928  |
| Cys | Leu   | Asn   | Ser   | Glu   | Gln   | Thr   | Leu   | Arg | Asn | Glu   | Met   | Lys   | Val   | Leu   | Leu   |      |
|     |       |       | 270   |       |       |       |       | 275 |     |       |       |       | 280   |       |       |      |
| atc | tta   | agc   | aag   | tgg   | ctg   | gaa   | cag   | gtg | tac | cca   | agc   | tcc   | gtg   | gag   | gaa   | 976  |
| Ile | Leu   | Ser   | Lys   | Trp   | Leu   | Glu   | Gln   | Val | Tyr | Pro   | Ser   | Ser   | Val   | Glu   | Glu   |      |
|     |       | 285   |       |       |       |       | 290   |     |     |       |       | 295   |       |       |       |      |
| gag | gca   | aag   | ctg   | ttt   | ttg   | tgg   | tgg   | cac | caa | gtc   | ctt   | cag   | ctc   | tcc   | ctc   | 1024 |
| Glu | Ala   | Lys   | Leu   | Phe   | Leu   | Trp   | Trp   | His | Gln | Val   | Leu   | G1n   | Leu   | Ser   | Leu   |      |
|     | 300   |       |       |       |       | 305   |       |     |     |       | 310   |       |       |       |       |      |
| att | cag   | aca   | gag   | cag   | aat   | gac   | tcc   | gtc | ctg | aca   | gaa   | tct   | gtc   | att   | cga   | 1072 |
| Ile | Gln   | Thr   | Glu   | Gln   | Asn   | Asp   | Ser   | Val | Leu | Thr   | Glu   | Ser   | Val   | Ile   | Arg   |      |
| 315 |       |       |       |       | 320   |       |       |     |     | 325   |       |       |       |       | 330   |      |
| att | ctg   | ctc   | ttg   | gtt   | cag   | agc   | agg   | cag | aac | ctc   | gtg   | gct   | gag   | g gag | aga   | 1120 |
| Ile | Leu   | Leu   | Leu   | Val   | Gln   | Ser   | Arg   | Gln | Asn | Leu   | Val   | Ala   | Glu   | ı Glu | Arg   |      |
|     |       |       |       | 335   | ,     |       |       |     | 340 |       | •     |       |       | 348   | 5     |      |
| cto | ago   | tct   | ggg   | ato   | cte   | ggg   | gca   | att | ggg | ttt   | ggc   | cgg   | g aag | g tc  | g cct | 1168 |
| Let | ı Sei | Ser   | Gly   | Ile   | e Lei | ıGly  | Ala   | Ile | Gly | Phe   | Gly   | Arg   | g Ly: | s Se  | r Pro |      |
|     |       |       | 350   | )     |       |       |       | 355 | •   |       |       |       | 36    | 0     |       |      |
| ttį | g tc  | t aa  | c agg | g tto | c cga | a gte | ggtt  | gcc | cga | ago   | ate   | g gc1 | t gc  | c tt  | c ctt | 1216 |
| Le  | u Se  | r Ası | n Arg | g Phe | e Arı | g Val | l Val | Ala | Arg | g Sei | r Met | t Ala | a Al  | a Ph  | e Leu |      |
|     |       | 36    | 5     |       |       |       | 370   | ) / | سرر |       |       | 37    | 5     |       |       |      |

| tca  | gtt   | cag   | gtt   | cct   | atg   | gaa   | gat   | cag   | atc   | cgt   | ttg   | agg  | cct   | ggc   | tct    | 1264 |
|------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|------|-------|-------|--------|------|
| Ser  | Val   | Gln   | Val   | Pro   | Met   | Glu   | Asp   | Gln   | Ile   | Arg   | Leu   | Arg  | Pro   | Gly   | Ser    |      |
|      | 380   |       |       |       |       | 385   |       |       |       |       | 390   |      |       |       |        |      |
| gaa  | tta   | cat   | ctg   | acc   | ccc   | aaa   | gct   | cag   | cag   | gct   | ctg   | aat  | gct   | ctt   | gaa    | 1312 |
| Glu  | Leu   | His   | Leu   | Thr   | Pro   | Lys   | Ala   | Gln   | Gln   | Ala   | Leu   | Asn  | Ala   | Leu   | Glu    |      |
| 395  |       |       |       |       | 400   |       |       |       |       | 405   |       |      |       |       | 410    |      |
| tcc  | atg   | gca   | tca   | agt   | aag   | cag   | tat   | gtt   | gaa   | tac   | cag   | gat  | caa   | ata   | ttg    | 1360 |
| Ser  | Met   | Ala   | Ser   | Ser   | Lys   | Gln   | Tyr   | Val   | Glu   | Tyr   | Gln   | Asp  | Gln   | Ile   | Leu    |      |
|      |       |       |       | 415   |       |       |       |       | 420   |       |       |      |       | 425   |        |      |
| caa  | gcc   | acc   | caa   | ttt   | ata   | agg   | cat   | cct   | ggc   | cat   | tgc   | ctt  | caa   | gat   | ggg    | 1408 |
| Gln  | Ala   | Thr   | Gln   | Phe   | Ile   | Arg   | His   | Pro   | Gly   | His   | Cys   | Leu  | Gln   | Asp   | Gly    |      |
|      |       |       | 430   |       |       |       |       | 435   |       |       |       |      | 440   |       |        | ,    |
| aaa  | agc   | ttc   | ttg   | gct   | ctt   | ctc   | gtt   | aac   | tgt   | ctg   | tat   | cca  | gaa   | gtg   | cat    | 1456 |
| Lys  | Ser   | Phe   | Leu   | Ala   | Leu   | Leu   | Val   | Asn   | Cys   | Leu   | Tyr   | Pro  | Glu   | Val   | His    |      |
|      |       | 445   |       |       |       |       | 450   |       |       |       |       | 455  |       |       |        |      |
| tat  | ttg   | gac   | cac   | ata   | cga   | tagi  | tta a | acact | tgagg | gc to | cttga | aaaa | a cc  | catte | gctg   | 1510 |
| Tyr  | Leu   | Asp   | His   | Ile   | Arg   |       |       |       |       |       |       |      |       |       |        |      |
|      | 460   |       |       |       |       |       |       |       |       |       |       |      |       |       |        |      |
| ttta | atgti | tta d | catti | taact | tt tg | gctgi | ttgca | a caa | agtaa | actt  | tgc   | tcaa | ttg   | cact  | gtagag | 1570 |
| ctca | agtti | tgg ( | ccaat | tgtg  | ta gi | ttgad | etga  | g at  | gcaag | gttg  | ggag  | ggcg | tta į | gata  | ttagat | 1630 |
| aat  | tttgg | ggg 1 | tgtgi | tgtg  | tg ta | gtgtg | gtgtį | g tgi | tttt  | ctta  | gcto  | ctta | aga ( | cctt  | ctgggg | 1690 |
| acto | cttta | aag 1 | tttt  | tata  | tt ta | atcca | acaa  | g aga | aaacı | ttac  | taa   | gttc | cac   | ttgg  | gtgcag | 1750 |
| agc  | cacto | cac a | agtt  | gccga | aa ta | gtcc  | cagto | c ato | ctca  | caag  | acc   | tcca | gat   | ggag  | ttcttt | 1810 |
| gta  | tgtt  | tcc a | actt  | ctgt  | ct c  | tgtti | ttat  | g taa | aatg  | ttcc  | aga   | tctg | aca : | acct  | tggaag | 1870 |
| tca  | ctca  | gta ( | cct   | tact  | tt ta | aaac  | cca   | t tt: | gtgt  | tcct  | cca   | aagt | aaa j | gaag  | tcaatt | 1930 |

| ttgaaaaatt | tctgcatttc | tcaaatgtgg | acaaatacaa | tagttttaaa | gtattgtttt | 1990 |
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| tctcagaagg | gagataaaaa | tgccgagtta | gttaaagtgg | gtcatgtgta | aaatacgacc | 2050 |
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| gtatcctcat | ggagaagctg | cctgtctgaa | tcaggatggc | aagctggcag | tctgggagga | 2170 |
| gcatgttttg | cacagatgtt | ttgtttggtc | cacttggtga | ggagtgcaga | cagggctgcc | 2230 |
| tctctctagt | cgggagagtc | tgtgcattcc | ctcgggccct | gaccctagcc | tcattcacat | 2290 |
| cacttgcccc | tgtcgacacc | taagtttgca | ccctttgata | gacaccatgt | tcgatatctg | 2350 |
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| tgcttgtttt | ttaacttcaa | actcagatga | agccaatgga | cctgctgaaa | cacttgtctg | 2470 |
| tggaaactgg | gtcaggtcgg | gagatctact | gaaatttggc | ttttttcca  | tagccacgtg | 2530 |
| ccttctgttg | ttgacagttc | attcattacc | aaagcctgtg | tgtaactttg | ccttgttctg | 2590 |
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| cgttcctcat | tctatcagct | ctagatggat | tttgcctgca | tagctggctt | aatatgtctt | 2710 |
| tgtgtatggg | tagtctgtag | cctgagaata | tttacctaaa | aatgtctaaa | cagccaccaa | 2770 |
| gaatgtttat | aggggtatag | gaatatagtt | aacagagtgc | taatctctcc | tcaaatgtcc | 2830 |
| ttttggaatg | cttcccccaa | aattgggaag | ttggtaggag | cttttcttta | ctttgaattt | 2890 |
| ctttacttgg | acagaacgat | tctgccttaa | agacacgctt | tgcagctctg | ataaagaaca | 2950 |
| tccctgttta | gtctcttgag | ttttacaggc | cacaaaatgt | ccgtctcaga | gggatctgtc | 3010 |
| tcagcttttc | ttatttttgc | ttctctccgt | tttcaaaatt | aatcatcttg | ttctctgtat | 3070 |
| aagaaaattt | gagaagctgt | ggacaattta | atagtctgat | ctggcaacag | cgatttttgt | 3130 |
| ttggaaátat | tttgtgtttt | ctttgaggag | gatataatta | ctgatatcct | aggatgtgaa | 3190 |
| atttttgagt | gacagtatgc | acattttaaa | gaaaattatg | attaatctgt | ataatgtttt | 3250 |
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| <212 | !> DN | <b>JA</b> |       |       |       |                 |      |       |       |      |      |       |       |       |        |     |
| <213 | 3> Hc | omo s     | sapie | ens   |       |                 |      |       |       |      |      |       | •     |       |        |     |
| <220 | )>    |           |       |       |       |                 |      |       |       |      |      |       |       |       |        |     |
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| aaca | ctga  | aca g     | gcgtg | gagco | cc go | ggcg            | gcte | g ctg | gccat | tggt | ggct | tggcg | ggc o | egggt | tgcagc | 60  |
| atg  | tct   | aga       | ctg   | gga   | gcc   | ctg             | ggt  | ggt   | gcc   | cgt  | gcc  | ggg   | ctg   | gga   | ctg    | 108 |
| Met  | Ser   | Arg       | Leu   | Gly   | Ala   | Leu             | Gly  | Gly   | Ala   | Arg  | Ala  | Gly   | Leu   | Gly   | Leu    |     |
| 1    |       |           |       | 5     |       |                 |      |       | 10    |      |      |       | •     | 15    |        |     |
| ttg  | ctg   | ggt       | acc   | gcc   | gcc   | ggc             | ctt  | gga   | ttc   | ctg  | tgc  | ctc   | ctt   | tac   | agc    | 156 |
| Leu  | Leu   | Gly       | Thr   | Ala   | Ala   | Gly             | Leu  | Gly   | Phe   | Leu  | Cys  | Leu   | Leu   | Tyr   | Ser    |     |
|      |       |           | 20    |       |       |                 |      | 25    |       |      |      |       | 30    |       |        |     |
| cag  | cga   | tgg       | aaa   | cgg   | acc   | cag             | cgt  | cat   | ggc   | cgc  | agc  | cag   | agc   | ctg   | ccc    | 204 |
| Gln  | Arg   | Trp       | Lys   | Arg   | Thr   | Gln             | Arg  | His   | Gly   | Arg  | Ser  | Gln   | Ser   | Leu   | Pro    |     |
|      |       | 35        |       |       |       |                 | 40   |       |       |      |      | 45    |       |       |        |     |
| aac  | tcc   | ctg       | gac   | tat   | acg   | cag             | act  | tca   | gat   | ccc  | gga  | cgc   | cac   | gtg   | atg    | 252 |
| Asn  | Ser   | Leu       | Asp   | Tyr   | Thr   | Gln             | Thr  | Ser   | Asp   | Pro  | Gly  | Arg   | His   | Val   | Met    |     |
|      | 50    |           |       |       |       | 55              |      |       |       |      | 60   |       |       |       |        |     |
| ctc  | ctg   | cgg       | gct   | gtc   | cca   | ggt             | ggg  | gct   | gga   | gat  | gcc  | tca   | gtg   | ctg   | ccc    | 300 |
| Leu  | Leu   | Arg       | Ala   | Val   | Pro   | Gly             | Gly  | Ala   | Gly   | Asp  | Ala  | Ser   | Val   | Leu   | Pro    |     |
| 65   |       |           |       |       | 70    |                 |      |       |       | 75   |      |       |       |       | 80     |     |
| agc  | ctt   | cca       | cgg   | gaa   | gga   | cag             | gag  | aag   | gtg   | ctg  | gac  | cgc   | ctg   | gac   | ttt    | 348 |
| Sar  | Lau   | Dro       | Ara   | Clu   | C1 v  | Cl <sub>n</sub> | C1   | 1     | Va1   | I    | A    | A     | 1     | A     | DI.    |     |

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|     |     |       |     | 85  |       |     |     |       | 90    |       |       |       |       | 95  |     |   |     |
|-----|-----|-------|-----|-----|-------|-----|-----|-------|-------|-------|-------|-------|-------|-----|-----|---|-----|
| gtg | ctg | acc   | agc | ctt | gtg   | gcg | ctg | cgg   | cgg   | gag   | gtg   | gag   | gag   | ctg | aga | 3 | 396 |
| Val | Leu | Thr   | Ser | Leu | Val   | Ala | Leu | Arg   | Arg   | Glu   | Val   | Glu   | Glu   | Leu | Arg |   |     |
|     |     |       | 100 |     |       |     |     | 105   |       |       |       |       | 110   |     |     |   |     |
| agc | agc | ctg   | cga | ggg | ctt   | gcg | ggg | gag   | att   | gtt   | ggg   | gag   | gtc   | cga | tgc | 4 | 144 |
| Ser | Ser | Leu   | Arg | Gly | Leu   | Ala | Gly | Glu   | Ile   | Val   | Gly   | Glu   | Val   | Arg | Cys |   |     |
|     |     | 115   |     |     |       |     | 120 |       |       |       |       | 125   |       |     |     |   |     |
| cac | atg | gaa   | gag | aac | cag   | aga | gtg | gct   | cgg   | cgg   | cga   | agg   | ttt   | ccg | ttt | 4 | 192 |
| His | Met | Glu   | Glu | Asn | Gln   | Arg | Val | Ala   | Arg   | Arg   | Arg   | Arg   | Phe   | Pro | Phe |   |     |
|     | 130 |       |     |     |       | 135 |     |       |       |       | 140   |       |       |     |     |   |     |
| gtc | cgg | gag   | agg | agt | gac   | tcc | act | ggc   | tcc   | agc   | tct   | gtc   | tac   | ttc | acg | ! | 540 |
| Val | Arg | Glu   | Arg | Ser | Asp   | Ser | Thr | Gly   | Ser   | Ser   | Ser   | Val   | Tyr   | Phe | Thr | • |     |
| 145 |     |       |     |     | 150   |     |     |       |       | 155   |       |       |       |     | 160 |   |     |
| gcc | tcc | tcg   | gga | gcc | acg   | ttc | aca | gat   | gct   | gag   | agt   | gaa   | ggg   | ggt | tac |   | 588 |
| Ala | Ser | Ser   | Gly | Ala | Thr   | Phe | Thr | Asp   | Ala   | Glu   | Ser   | Glu   | Gly   | Gly | Tyr |   |     |
|     |     |       |     | 165 |       |     |     |       | 170   |       |       |       |       | 175 |     |   |     |
| aca | aca | ġcc   | aat | gcg | gag   | tct | gac | aat   | gag   | cgg   | gac   | tct   | gac   | aaa | gaa |   | 636 |
| Thr | Thr | Ala   | Asn | Ala | Glu   | Ser | Asp | Asn   | Glu   | Arg   | Asp   | Ser   | Asp   | Lys | Glu |   |     |
|     |     |       | 180 |     |       |     |     | 185   |       |       |       |       | 190   |     |     |   |     |
| agt | gag | gac   | ggg | gaa | gat   | gaa | gtg | ago   | tgt   | gag   | act   | gtg   | aag   | atg | ggg |   | 684 |
| Ser | Glu | Asp   | Gly | Glu | Asp   | Glu | Val | Ser   | Cys   | Glu   | Thr   | Val   | Lys   | Met | Gly |   |     |
|     |     | 195   | •   |     |       |     | 200 | )     |       |       |       | 205   | j     |     |     |   |     |
| aga | aag | g gat | tct | ctt | gac   | ttg | gag | g gaa | gag   | g gca | gct   | t tca | a ggt | gcc | tcc |   | 732 |
| Arg | Lys | s Asp | Ser | Leu | ı Asp | Leu | Glu | ı Glu | ı Glu | ı Ala | . Ala | a Sei | Gly   | Ala | Ser |   |     |
|     | 210 | )     |     |     |       | 215 | 5   | /     | تنمن  |       | 220   | )     |       |     |     |   |     |

| agt | gcc | ctg | gag | gct | gga | ggt | tcc | tca | ggc   | ttg | gag | gat | gtg | ctg | ccc | 780  |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-------|-----|-----|-----|-----|-----|-----|------|
| Ser | Ala | Leu | Glu | Ala | Gly | Gly | Ser | Ser | Gly   | Leu | Glu | Asp | Val | Leu | Pro |      |
| 225 |     |     |     |     | 230 |     | •   |     |       | 235 |     |     |     |     | 240 |      |
| ctc | ctg | cag | cag | gcc | gac | gag | ctg | cac | agg   | ggt | gat | gag | caa | ggc | aag | 828  |
| Leu | Leu | Gln | Gln | Ala | Asp | Glu | Leu | His | Arg   | Gly | Asp | Glu | Gln | Gly | Lys |      |
|     |     |     |     | 245 |     |     |     |     | 250   |     |     |     |     | 255 |     |      |
| cgg | gag | ggc | ttc | cag | ctg | ctg | ctc | aac | aac   | aag | ctg | gtg | tat | gga | agc | 876  |
| Arg | Glu | Gly | Phe | Gln | Leu | Leu | Leu | Asn | Asn   | Lys | Leu | Val | Tyr | Gly | Ser |      |
|     |     |     | 260 |     |     |     |     | 265 |       |     |     |     | 270 |     |     |      |
| cgg | cag | gac | ttt | ctc | tgg | cgc | ctg | gcc | cga   | gcc | tac | agt | gac | atg | tgt | 924  |
| Arg | Gln | Asp | Phe | Leu | Trp | Arg | Leu | Ala | Arg   | Ala | Tyr | Ser | Asp | Met | Cys |      |
|     |     | 275 |     |     |     |     | 280 |     |       |     |     | 285 |     |     |     |      |
| gag | ctc | act | gag | gag | gtg | agc | gag | aag | aag   | tca | tat | gcc | cta | gat | gga | 972  |
| Glu | Leu | Thr | Glu | Glu | Val | Ser | Glu | Lys | Lys   | Ser | Tyr | Ala | Leu | Asp | Gly |      |
|     | 290 |     |     |     |     | 295 |     |     |       |     | 300 |     |     |     |     |      |
| aaa | gaa | gaa | gca | gag | gct | gct | ctg | gag | aag   | ggg | gat | gag | agt | gct | gac | 1020 |
| Lys | Glu | Glu | Ala | Glu | Ala | Ala | Leu | Glu | Lys   | Gly | Asp | Glu | Ser | Ala | Asp |      |
| 305 |     |     | •   |     | 310 |     |     |     |       | 315 |     |     |     |     | 320 |      |
| tgt | cac | ctg | tgg | tat | gcg | gtg | ctt | tgt | ggt   | cag | ctg | gct | gag | cat | gag | 1068 |
| Cys | His | Leu | Trp | Tyr | Ala | Val | Leu | Cys | Gly   | Gln | Leu | Ala | Glu | His | Glu |      |
|     |     |     |     | 325 |     |     |     |     | 330   |     |     |     |     | 335 |     |      |
| agc | atc | cag | agg | cgc | atc | cag | agt | ggc | ttt   | agc | ttc | aag | gag | cat | gtg | 1116 |
| Ser | Ile | Gln | Arg | Arg | Ile | Gln | Ser | Gly | Phe   | Ser | Phe | Lys | Glu | His | Val |      |
|     |     |     | 340 |     |     |     |     | 345 | - نشي |     |     |     | 350 |     |     |      |
| gac | aaa | gcc | att | gct | ctc | cag | cca | gaa | aac   | ссс | atg | gct | cac | ttt | ctt | 1164 |

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| Asp | Lys  | Ala | He   | Ala   | Leu  | Gln  | Pro  | Glu   | Asn        | Pro  | Met  | Ala  | His  | Phe  | Leu     |      |
|-----|------|-----|------|-------|------|------|------|-------|------------|------|------|------|------|------|---------|------|
|     |      | 355 |      |       |      |      | 360  |       |            |      | ٠.   | 365  |      |      |         |      |
| ctt | ggc  | agg | tgg  | tgc   | tat  | cag  | gtc  | tct   | cac        | ctg  | agc  | tgg  | cta  | gaa  | aaa     | 1212 |
| Leu | Gly  | Arg | Trp  | Cys   | Tyr  | Gln  | Val  | Ser   | His        | Leu  | Ser  | Trp  | Leu  | Glu  | Lys     |      |
|     | 370  |     |      |       |      | 375  |      |       |            |      | 380  |      |      |      |         |      |
| aaa | act  | gct | aca  | gcc   | ttg  | ctt  | gaa  | agc   | cct        | ctc  | agt  | gcc  | act  | gtg  | gaa     | 1260 |
| Lys | Thr  | Ala | Thr  | Ala   | Leu  | Leu  | Glu  | Ser   | Pro        | Leu  | Ser  | Ala  | Thr  | Val  | Glu     |      |
| 385 |      |     |      |       | 390  |      |      |       |            | 395  |      |      |      |      | 400     |      |
| gat | gcc  | ctc | cag  | agc   | ttc  | cta  | aag  | gct   | gaa        | gaa  | cta  | cag  | cca  | gga  | ttt     | 1308 |
| Asp | Ala  | Leu | Gln  | Ser   | Phe  | Leu  | Lys  | Ala   | Glu        | Glu  | Leu  | Gln  | Pro  | Gly  | Phe     |      |
|     |      |     |      | 405   |      |      |      |       | 410        |      |      |      |      | 415  |         |      |
| tcc | aaa  | gca | gga  | agg   | gta  | tat  | att  | tcc   | aag        | tgc  | tac  | aga  | gaa  | cta  | ggg     | 1356 |
| Ser | Lys  | Ala | Gly  | Arg   | Val  | Tyr  | Ile  | Ser   | Lys        | Cys  | Tyr  | Arg  | Glu  | Leu  | Gly     |      |
|     |      |     | 420  |       |      |      |      | 425   |            |      |      |      | 430  |      |         |      |
| aaa | aac  | tct | gaa  | gct   | aga  | tgg  | tgg  | atg   | aag        | ttg  | gcc  | ctg  | gag  | ctg  | cca     | 1404 |
| Lys | Asn  | Ser | Glu  | Ala   | Arg  | Trp  | Trp  | Met   | Lys        | Leu  | Ala  | Leu  | Glu  | Leu  | Pro     |      |
|     |      | 435 |      |       |      |      | 440  |       |            |      |      | 445  |      |      |         |      |
| gat | gtc  | acg | aag  | gag   | gat  | ttg  | gct  | atc   | cag        | aag  | gac  | ctg  | gaa  | gaa  | ctg     | 1452 |
| Asp | Val  | Thr | Lys  | Glu   | Asp  | Leu  | Ala  | Ile   | Gln        | Lys  | Asp  | Leu  | Glu  | Glu  | Leu     |      |
|     | 450  |     |      |       |      | 455  |      |       |            |      | 460  | 1    |      |      |         |      |
| gaa | gtc  | att | tta  | cga   | gac  | taa  | ccac | gtt   | tcac       | tggc | ct t | catg | actt | g    |         | 1500 |
| Glu | Val  | Ile | Leu  | Arg   | Asp  | 1    |      |       |            |      |      |      |      |      |         |      |
| 465 | -    |     |      |       | 470  | )    |      |       |            |      |      |      |      |      |         |      |
| atg | ccac | tat | ttaa | iggtg | gg g | gggc | gggg | a gg  | cttt<br>سر | tttc | ctt  | agac | ctt  | gctg | gagatca | 1560 |
| gga | aaco | aca | caaa | itcte | tc t | ccte | ggto | t gʻa | ctgo       | tacc | cac  | taco | act  | cccc | attagt  | 1620 |

| taatttattc | taacctctaa | cctaatctag | aattggggca | gtactcatgg | cttccgtttc | 1680 |
|------------|------------|------------|------------|------------|------------|------|
| tgttgttctc | tcccttgagt | aatctcttaa | aaaaatcaag | attcacacct | gccccaggat | 1740 |
| tacacatggg | tagagcctgc | aagacctgag | accttccaat | tgctggtgag | gtggatgaac | 1800 |
| ttcaaagcta | taggaacaaa | gcacataact | tgtcacttta | atcttttca  | ctgactaata | 1860 |
| ggactcagta | catatagtct | taagatcata | ccttacctac | caaggtaaaa | agagggatca | 1920 |
| gagtggccca | cagacattgc | tttcttatca | cctatcatgt | gaattctacc | tgtattcctg | 1980 |
| ggctggacca | cttgataact | tccagtgtcc | tggcagcttt | tggaatgaca | gcagtggtat | 2040 |
| ggggtttatg | atgctataaa | acaatgtctg | aaaagttgcc | tagaatatat | tttgttacaa | 2100 |
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<212> DNA

<213> Homo sapiens

<220>

<221> CDS

⟨222⟩ (74)... (805)

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cccacaagga gca atg gag cag ggc agc ggc cgc ttg gag gac ttc cct 109
Met Glu Gln Gly Ser Gly Arg Leu Glu Asp Phe Pro

1 5 10

gtc aat gtg ttc tcc gtc act cct tac aca ccc agc acc gct gac atc

157

Val Asn Val Phe Ser Val Thr Pro Tyr Thr Pro Ser Thr Ala Asp Ile

15

20

25

| cag | gtg | tcc | gat | gat  | gac  | aag                                     | gcg | ggg | gcc        | acc        | ttg | ctc | ttc | tca | ggc  | 205 |
|-----|-----|-----|-----|------|------|---|-----|-----|------------|------------|-----|-----|-----|-----|------|-----|
| Gln | Val | Ser | Asp | Asp  | Asp  | Lys                                     | Ala | Gly | Ala        | Thr        | Leu | Leu | Phe | Ser | Gly  |     |
|     | 30  |     |     |      |      | 35                                      |     |     |            |            | 40  |     |     |     |      | . • |
| atc | ttt | ctg | gga | ctg  | gtg  | ggg                                     | atc | aca | ttc        | act        | gtc | atg | ggc | tgg | atc  | 253 |
| Ile | Phe | Leu | Gly | Leu  | Val  | Gly                                     | Ile | Thr | Phe        | Thr        | Val | Met | Gly | Trp | Ile  |     |
| 45  |     |     |     |      | 50   |   |     |     |            | 55         |     |     |     |     | 60   |     |
| aaa | tac | caa | ggt | gtc  | tcc  | cac                                     | ttt | gaa | tgg        | acc        | cag | ctc | ctt | ggg | ccc  | 301 |
| Lys | Tyr | Gln | Gly | Val  | Ser  | His                                     | Phe | Glu | Trp        | Thr        | Gln | Leu | Leu | Gly | Pro  |     |
|     |     |     |     | 65   |      |   |     |     | 70         |            |     |     |     | 75  |      |     |
| gtc | ctg | ctg | tca | gtt  | ggg  | gtg                                     | aca | ttc | atc        | ctg        | att | gct | gtg | tgc | aag  | 349 |
|     |     |     | Ser |      |      |   |     |     |            |            |     |     |     |     |      |     |
|     |     |     | 80  |      | •    |   |     | 85  |            |            |     |     | 90  | •   | •    |     |
| ttc | aaa | atg | ctc | tcc  | tgc  | cag                                     | ttg | tgc | aaa        | gaa        | agt | gag |     | agg | gtc  | 397 |
|     |     |     | Leu |      |      |   |     |     |            |            |     |     |     |     |      |     |
|     | _,_ | 95  | 200 |      | 0,0  | • | 100 | 0,0 | 2,2        | <b>313</b> | 001 | 105 | 014 | 6   | , 41 |     |
| cca | gar |     | gaa | cag  | aca  | cca                                     |     | aas | cca        | toa        | +++ |     | tto | act | aac  | 445 |
|     |     |     |     |      |      |   |     |     |            |            |     |     |     |     |      | 440 |
| 110 |     | Sei | Glu | GIII | 1111 |   | Gly | GIY | rro        | ser        |     | vai | rne | HIL | GIY  |     |
|     | 110 |     |     |      |      | 115                                     |     |     |            |            | 120 |     |     |     |      |     |
| atc | aac | caa | ccc | atc  | acc  | ttc                                     | cat | ggg | gcc        | act        | gtg | gtg | cag | tac | atc  | 493 |
| Ile | Asn | Gln | Pro | Ile  | Thr  | Phe                                     | His | Gly | Ala        | Thr        | Val | Val | Gln | Tyr | Ile  |     |
| 125 |     |     |     |      | 130  |   |     |     |            | 135        |     |     |     |     | 140  |     |
| cct | cct | cct | tat | ggt  | tct  | cca                                     | gag | cct | atg        | ggg        | ata | aat | acc | agc | tac  | 541 |
| Pro | Pro | Pro | Tyr | Gly  | Ser  | Pro                                     | Glu | Pro | Met        | Gly        | Ile | Asn | Thr | Ser | Tyr  |     |
|     |     |     |     | 145  |      |   |     |     | 150        |            |     |     |     | 155 | ı    |     |
| ctg | cag | tct | gtg | gtg  | agc  | ccc                                     | tgc | ggc | ندر<br>ctc | ata        | acc | tct | gga | ggg | gca  | 589 |
|     |     |     |     |      |      |   |     |     |            |            |     |     |     |     |      |     |

| Leu | Gln  | Ser | Val  | Val  | Ser  | Pro  | Cys  | Gly  | Leu  | Ile  | Thr  | Ser  | Gly  | Gly  | Ala    |      |
|-----|------|-----|------|------|------|------|------|------|------|------|------|------|------|------|--------|------|
|     |      |     | 160  |      |      |      |      | 165  |      |      |      |      | 170  |      |        |      |
| gca | gcc  | gcc | atg  | tca  | agt  | cct  | cct  | caa  | tac  | tac  | acc  | atc  | tac  | cct  | caa    | 637  |
| Ala | Ala  | Ala | Met  | Ser  | Ser  | Pro  | Pro  | Gln  | Tyr  | Tyr  | Thr  | Ile  | Tyr  | Pro  | Gln    |      |
|     |      | 175 |      |      |      |      | 180  |      |      |      |      | 185  |      |      |        |      |
| gat | aac  | tct | gca  | ttt  | gtg  | gtt  | gat  | gag  | ggc  | tgc  | ctt  | tct  | ttc  | acg  | gac    | 685  |
| Asp | Asn  | Ser | Ala  | Phe  | Val  | Val  | Asp  | Glu  | Gly  | Cys  | Leu  | Ser  | Phe  | Thr  | Asp    |      |
|     | 190  |     |      |      |      | 195  |      |      |      |      | 200  |      |      |      |        |      |
| ggt | gga  | aat | cac  | agg  | ссс  | aat  | cct  | gat  | gtt  | gac  | cag  | cta  | gaa  | gag  | aca    | 733  |
| Gly | Gly  | Asn | His  | Arg  | Pro  | Asn  | Pro  | Asp  | Val  | Asp  | Gln  | Leu  | Glu  | Glu  | Thr    |      |
| 205 |      |     |      |      | 210  |      |      |      |      | 215  |      |      |      |      | 220    |      |
| cag | ctg  | gaa | gag  | gag  | gcc  | tgt  | gcc  | tgc  | ttc  | tct  | cct  | ссс  | cct  | tat  | gaa    | 781  |
| Gln | Leu  | Glu | Glu  | Glu  | Ala  | Cys  | Ala  | Cys  | Phe  | Ser  | Pro  | Pro  | Pro  | Tyr  | Glu    |      |
|     |      |     |      | 225  |      |      |      |      | 230  |      |      |      |      | 235  |        |      |
| gaa | ata  | tac | tct  | ctc  | cct  | cgc  | tag  | aggc | t at | tctg | atat | aat  | aaca | caa  |        | 830  |
| Glu | Ile  | Tyr | Ser  | Leu  | Pro  | Arg  |      |      |      |      |      |      |      |      |        |      |
|     |      |     | 240  |      |      |      |      |      |      |      |      |      |      |      |        |      |
| tgc | tcag | ctc | aggg | agca | ag t | gttt | ccgt | c at | tgtt | acct | gac  | aacc | gtg  | gtgt | tctatg | 890  |
| ttg | taac | ctt | caga | agtt | ac a | gcag | cgcc | c ag | gcag | cctg | aca  | gaga | tca  | ttca | aggggg | 950  |
| gaa | aggg | gaa | gtgg | gagg | tg c | aatt | tctc | a ga | ttgg | taaa | aat  | tagg | ctg  | ggct | ggggaa | 1010 |
| att | ctcc | tcc | ggaa | cagt | tt c | aaat | tccc | t cg | ggta | agaa | atc  | tcct | gta  | taag | gttcag | 1070 |
| gag | cagg | aat | ttca | cttt | tt c | atcc | acca | с сс | tccc | cctt | ctc  | tgta | gga  | aggc | attggt | 1130 |
| ggc | tcaa | ttt | taac | ccca | gc a | gcca | atgg | a aa | aatc | acga | ctt  | ctga | gac  | tttg | ggagtt | 1190 |
| tcc | acag | agg | tgag | agtc | gg g | tggg | aagg | a ag | cagg | gaag | aga  | aagc | agg  | ccca | gctgga | 1250 |
| gat | ttcc | tgg | tggc | tgtc | ct t | ggcc | ccaa | a gc | agac | tcac | taa  | tccc | aaa  | caac | tcagct | 1310 |

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| gccatctggc | ctctctgagg | actctgggta | ccttaaagac | tataaaacaa | aacaaaacaa | 1370 |
|------------|------------|------------|------------|------------|------------|------|
| aaacatcaaa | ccaatgaaat | aaaataaatc | atgtctcctg | ctagaatagt | attggatacc | 1430 |
| tgactaaatt | acacaaaata | gaccataata | ggatagcact | gtgaatacat | ccttcccgat | 1490 |
| cactgagtca | cagtgaccct | tggctgctgc | agttctcgtc | tgcaaggttg | aagcttgacg | 1550 |
| tgtgatgaac | atgggtgggc | tcttggtcca | ccccaggctg | gggcctgcgc | caagcatgaa | 1610 |
| ctagctggga | ccagtggctg | acagaacaca | ggacttccct | aagtacccgt | aggtccgtgg | 1670 |
| agcaagacag | agcagagttg | ccatgtcaac | acatggggaa | tgatatgata | gaaacaatct | 1730 |
| ttatgactaa | aagaaactca | tcttcttcat | taaaaaaact | ttggtgtcct | t          | 1781 |

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<211> 1788

<212> DNA

<213> Homo sapiens

<220>

<221> CDS

<222> (87)...(899)

<400> 60

10

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Met Ala Gly Ala Glu Asp Trp Pro Gly

1 5

20

25

cag cag ctg gag ctg gac gag gac gag gcg tct tgt tgc cgc tgg ggc 161 Gln Gln Leu Glu Leu Asp Glu Asp Glu Ala Ser Cys Cys Arg Trp Gly

gcg cag cac gcc ggg gcc cgc gag ctg gct gcg ctc tac tcg cca ggc 209

15

| Ala | Gln | His | Ala | Gly   | Ala  | Arg | Glu | Leu              | Ala | Ala | Leu | Tyr | Ser | Pro | Gly |   |     |
|-----|-----|-----|-----|-------|------|-----|-----|------------------|-----|-----|-----|-----|-----|-----|-----|---|-----|
|     |     |     |     | . 30. |      |     |     |                  | 35  |     |     |     |     | 40  |     |   |     |
| aag | cgc | ctc | cag | gag   | tgg  | tgc | tct | gtg              | atc | ctg | tgc | ttc | agc | ctc | atc | 2 | 257 |
| Lys | Arg | Leu | Gln | Glu   | Trp  | Cys | Ser | Val <sup>-</sup> | Ile | Leu | Cys | Phe | Ser | Leu | Ile |   |     |
|     |     |     | 45  |       |      |     |     | 50               |     |     |     |     | 55  |     |     |   |     |
| gcc | cac | aac | ctg | gtc   | cat  | ctc | ctg | ctg              | ctg | gcc | cgc | tgg | gag | gac | aca | 3 | 305 |
| Ala | His | Asn | Leu | Val   | His  | Leu | Leu | Leu              | Leu | Ala | Arg | Trp | Glu | Asp | Thr |   |     |
|     |     | 60  |     |       |      |     | 65  |                  |     |     |     | 70  |     |     |     |   |     |
| ccc | ctc | gtc | ata | ctc   | ggt  | gtt | gtt | gca              | ggg | gct | ctc | att | gct | gac | ttc | ; | 353 |
| Pro | Leu | Val | Ile | Leu   | G1 y | Val | Val | Ala              | Gly | Ala | Leu | Ile | Ala | Asp | Phe |   |     |
|     | 75  |     |     |       |      | 80  |     |                  |     |     | 85  |     |     |     |     |   |     |
| ttg | tct | ggc | ctg | gta   | cac  | tgg | ggt | gct              | gac | aca | tgg | ggc | tct | gtg | gag | 4 | 401 |
| Leu | Ser | Gly | Leu | Val   | His  | Trp | Gly | Ala              | Asp | Thr | Trp | Gly | Ser | Val | Glu |   |     |
| 90  |     |     |     |       | 95   |     |     |                  |     | 100 |     |     |     |     | 105 |   |     |
| ctg | ccc | att | gtg | ggg   | aag  | gct | ttc | atc              | cga | ccc | ttc | cgg | gag | cac | cac | 4 | 149 |
| Leu | Pro | Ile | Val | Gly   | Lys  | Ala | Phe | Ile              | Arg | Pro | Phe | Arg | Glu | His | His |   |     |
|     |     |     |     | 110   |      |     |     |                  | 115 |     |     |     |     | 120 |     |   |     |
| att | gac | cca | aca | gct   | atc  | aca | cgg | cac              | gac | ttc | atc | gag | acc | aac | ggg | 4 | 497 |
| Ile | Asp | Pro | Thr | Ala   | Ile  | Thr | Arg | His              | Asp | Phe | Ile | Glu | Thr | Asn | Gly |   |     |
|     |     |     | 125 |       |      |     |     | 130              |     |     |     |     | 135 |     |     |   |     |
| gac | aac | tgc | ctg | gtg   | aca  | ctg | ctg | ccg              | ctg | cta | aac | atg | gcc | tac | aag | ! | 545 |
| Asp | Asn | Cys | Leu | Val   | Thr  | Leu | Leu | Pro              | Leu | Leu | Asn | Met | Ala | Tyr | Lys |   |     |
|     |     | 140 |     |       |      |     | 145 |                  |     |     |     | 150 |     |     |     |   |     |
| ttc | cgc | acc | cac | agc   | cct  | gaa | gcc | ctg              | gag | cag | cta | tac | ccc | tgg | gag |   | 593 |
| Phe | Arg | Thr | His | Ser   | Pro  | Glu | Ala | Leu              | Glu | Gln | Leu | Tvr | Pro | Trn | Glu |   | *   |

|     | 155  |     |      |      |      | 160  |      |      |            |      | 165 | •    |      |      |        |      |
|-----|------|-----|------|------|------|------|------|------|------------|------|-----|------|------|------|--------|------|
| tgc | ttc  | gtc | ttc  | tgc  | ctg  | atc  | atc  | ttc  | ggc        | acc  | ttc | acc  | aac  | cag  | atc    | 641  |
| Cys | Phe  | Val | Phe  | Cys  | Leu  | Ile  | Ile  | Phe  | Gly        | Thr  | Phe | Thr  | Asn  | Gln  | Ile    |      |
| 170 |      |     |      |      | 175  |      |      |      |            | 180  |     |      |      |      | 185    |      |
| cac | aag  | tgg | tcg  | cac  | acg  | tac  | ttt  | ggg  | ctg        | cca  | cgc | tgg  | gtc  | acc  | ctc    | 689  |
| His | Lys  | Trp | Ser  | His  | Thr  | Tyr  | Phe  | Gly  | Leu        | Pro  | Arg | Trp  | Val  | Thr  | Leu    |      |
|     |      |     |      | 190  |      |      |      |      | 195        |      |     |      |      | 200  |        |      |
| ctg | cag  | gac | tgg  | cat  | gtc  | atc  | ctg  | cca  | cgt        | aaa  | cac | cat  | cgc  | atc  | cac    | 737  |
| Leu | Gln  | Asp | Trp  | His  | Val  | Ile  | Leu  | Pro  | Arg        | Lys  | His | His  | Arg  | Ile  | His    |      |
|     |      |     | 205  |      |      |      |      | 210  |            |      |     |      | 215  |      |        |      |
| cac | gtc  | tca | ccc  | cac  | gag  | acc  | tac  | ttc  | tgc        | atc  | acc | aca  | ggc  | tgg  | ctc    | 785  |
| His | Val  | Ser | Pro  | His  | Glu  | Thr  | Tyr  | Phe  | Cys        | Ile  | Thr | Thr  | Gly  | Trp  | Leu    | ,    |
|     |      | 220 |      |      |      |      | 225  |      |            |      |     | 230  |      |      |        |      |
| aac | tac  | cct | ctg  | gag  | aag  | ata  | ggc  | ttc  | tgg        | cga  | cgc | ctg  | gag  | gac  | ctc    | 833  |
| Asn | Tyr  | Pro | Leu  | Glu  | Lys  | Ile  | Gly  | Phe  | Trp        | Arg  | Arg | Leu  | Glu  | Asp  | Leu    |      |
|     | 235  |     |      |      |      | 240  |      |      |            |      | 245 |      |      |      |        |      |
| atc | cag  | ggc | ctg  | acg  | ggc  | gag  | aag  | cct  | cgg        | gca  | gat | gac  | atg  | aaa  | tgg    | 881  |
| Ile | Gln  | Gly | Leu  | Thr  | Gly  | Glu  | Lys  | Pro  | Arg        | Ala  | Asp | Asp  | Met  | Lys  | Trp    |      |
| 250 |      |     |      |      | 255  |      |      |      |            | 260  |     |      |      |      | 265    |      |
| gcc | cag  | aag | atc  | aaa  | taa  | c tt | ctcc | gagc | ctg        | ctac | ctg | gttg | ccaa | cc   |        | 930  |
| Ala | Gln  | Lys | Ile  | Lys  |      |      |      |      |            |      |     |      |      |      |        |      |
|     |      | •   |      | 270  |      |      |      |      |            |      |     |      |      |      |        |      |
| ttc | ccta | gcc | ccca | aacc | ga a | gcca | tctg | c ca | aatt       | ccag | cct | cttt | gag  | ctgg | cccctc | 990  |
| cag | atgg | aga | ggac | atct | cc t | gggc | tggg | c cc | aggt<br>سر | accc | cag | ccca | ссс  | ctca | tgacac | 1050 |
| aga | atac | ttg | agcc | actg | at t | tttc | attt | c ťt | tttt       | tttt | ttt | ttcc | tcg  | gccc | ctcctc | 1110 |

| agccacctga | gttgctctat | ctgcaagcct | gactctgcca | gcctcccctg | gtagagagga | 1170 |
|------------|------------|------------|------------|------------|------------|------|
| ggtttaccca | ctccctgcac | gcctgccgtc | cctgccccgc | tgggcagccc | ttcagtgtgg | 1230 |
| ctggcgttgg | ggccagtgag | ttgcctcttt | ccctccttgt | ctggccccag | tggtctgggg | 1290 |
| agcccccagg | cacacctaag | cgtcgtggag | cattgttctg | ccacagccct | gcatactgac | 1350 |
| cccgggaggc | tgggcaggtg | gacagcccca | gccaccacct | tcagcctagc | ctgtcccca  | 1410 |
| aggatggtga | agctcagcag | gggtctgagg | gtagccggcc | agaagaggct | ggaacctcct | 1470 |
| gctcaagtct | agacccctac | ttctctgctg | ccccaccct  | gccagagctg | atgtttccaa | 1530 |
| taccaagatg | tcttcacagg | gcacagcccc | tgcagagcat | cttggtcatt | tggaagagga | 1590 |
| cacggtatcc | cctctggcca | gagtatgtca | gagaaggaag | agtagggctt | ttttgttttg | 1650 |
| tttttttta  | aaggtgcttg | cttgtttaat | gtaaataata | gaaagcctta | atatcttttc | 1710 |
| tgtaacacgg | agtaatattt | taatgtcatg | ttttggatgt | acataatata | tttataacaa | 1770 |
| agcagcaaga | gtctactt   |            |            |            |            | 1788 |

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<213> Homo sapiens

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Met Asp Arg Gly Glu Lys Ile Gln Leu Lys Arg Val Phe Gly Tyr Trp

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20 25 30

Val Ser Pro Lys Gly Val Leu Ala Tyr Ser Cys Met Asn Val Gly Val

35 40 <sub>20</sub> 45

Ser Leu Cys Val Trp Ala Gly Cys Ala Ile Leu Ala Met Thr Ser Thr

|     | 50  |     |     |     |     | 55  |     |     |             |     | 60  |     |     |     |     |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-------------|-----|-----|-----|-----|-----|-----|
| Leu | Cys | Ser | Ala | Glu | Ile | Ser | Ile | Ser | Phe         | Pro | Cys | Ser | Gly | Ala | Gln |
| 65  |     |     |     |     | 70  |     |     |     |             | 75  |     |     |     |     | 80  |
| Tyr | Tyr | Phe | Leu | Lys | Arg | Tyr | Phe | Gly | Ser         | Thr | Val | Ala | Phe | Leu | Asn |
|     |     |     |     | 85  |     |     |     |     | 90          |     |     |     |     | 95  |     |
| Leu | Trp | Thr | Ser | Leu | Phe | Leu | Gly | Ser | Gly         | Val | Val | Ala | Gly | Gln | Ala |
|     |     |     | 100 |     |     |     |     | 105 |             |     |     |     | 110 |     |     |
| Leu | Leu | Leu | Ala | Glu | Tyr | Ser | Ile | Gln | Pro         | Phe | Phe | Pro | Ser | Cys | Ser |
|     |     | 115 |     |     |     |     | 120 |     |             |     |     | 125 |     |     |     |
| Val | Pro | Lys | Leu | Pro | Lys | Lys | Cys | Leu | Ala         | Leu | Ala | Met | Leu | Trp | Ile |
|     | 130 |     |     |     |     | 135 |     |     |             |     | 140 |     |     |     |     |
| Val | Gly | Ile | Leu | Thr | Ser | Arg | Gly | Val | Lys         | Glu | Val | Thr | Trp | Leu | Gln |
| 145 |     |     |     |     | 150 |     |     |     |             | 155 |     |     |     |     | 160 |
| Ile | Ala | Ser | Ser | Val | Leu | Lys | Val | Ser | Ile         | Leu | Ser | Phe | Ile | Ser | Leu |
|     |     |     |     | 165 |     |     |     |     | 170         |     |     |     |     | 175 |     |
| Thr | Gly | Val | Val | Phe | Leu | Ile | Arg | Gly | Lys         | Lys | Glu | Asn | Val | Glu | Arg |
|     |     |     | 180 |     |     |     |     | 185 |             |     |     |     | 190 |     |     |
| Phe | Gln | Asn | Ala | Phe | Asp | Ala | Glu | Leu | Pro         | Asp | Ile | Ser | His | Leu | Ile |
|     |     | 195 |     |     |     |     | 200 |     |             |     |     | 205 |     |     |     |
| Gln | Ala | Ile | Phe | Gln | Gly | Tyr | Phe | Ala | Tyr         | Ser | Gly | Glu | Leu | Lys | Lys |
|     | 210 |     |     |     |     | 215 |     |     |             |     | 220 |     |     |     |     |
| Pro | Arg | Thr | Thr | Ile | Pro | Lys | Cys | Ile | Phe         | Thr | Ala | Leu | Pro | Leu | Val |
| 225 |     |     |     |     | 230 | ı   |     |     |             | 235 | i   |     |     |     | 240 |
| Thr | Val | Val | Tyr | Leu | Leu | Val | Asn | Ile | e Ser<br>نر | Tyr | Leu | Thr | Val | Leu | Thr |
|     |     |     |     | 245 |     |     |     | /   | 250         | )   |     |     |     | 255 | ,   |

Pro Arg Glu Ile Leu Ser Ser Asp Ala Val Ala Ile Thr Trp Ala Asp 260 265 270 Arg Ala Phe Pro Ser Leu Ala Trp Ile Met Pro Phe Ala Ile Ser Thr 275 280 285 Ser Leu Phe Ser Asn Leu Leu Ile Ser Ile Phe Lys Ser Ser Arg Pro 290 295 300 Ile Tyr Leu Ala Ser Gln Glu Gly Gln Leu Pro Leu Leu Phe Asn Thr 305 310 315 320 Leu Asn Ser His Ser Ser Pro Phe Thr Ala Val Leu Leu Leu Val Thr 325 330 335 Leu Gly Ser Leu Ala Ile Ile Leu Thr Ser Leu Ile Asp Leu Ile Asn 340 345 350 Tyr Ile Phe Phe Thr Gly Ser Leu Trp Ser Ile Leu Leu Met Ile Gly 355 360 365 Ile Leu Arg Arg Arg Tyr Gln Glu Pro Asn Leu Ser Ile Pro Tyr Lys 370 375 380 Val Lys Leu Asp Phe 385 <210> 62

<211> 348

<212> PRT

<213> Homo sapiens

<400> 62

Met Ala Ala Thr Leu Gly Pro Leu Gly Ser Trp Gln Gln Trp Arg Arg

| 1   |     |     |     | 5   |     |     |     |     | 10          |     |     |     |       | 15  |     |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-------------|-----|-----|-----|-------|-----|-----|
| Cys | Leu | Ser | Ala | Arg | Asp | Gly | Ser | Arg | Met         | Leu | Leu | Leu | Leu   | Leu | Leu |
|     |     |     | 20  |     |     |     |     | 25  |             |     |     | -   | 30    |     |     |
| Leu | Gly | Ser | Gly | Gln | Gly | Pro | Gln | Gln | Val         | Gly | Ala | Gly | Gln   | Thr | Phe |
|     |     | 35  |     |     |     |     | 40  |     |             |     |     | 45  |       |     |     |
| Glu | Tyr | Leu | Lys | Arg | Glu | His | Ser | Leu | Ser         | Lys | Pro | Tyr | Gln   | Gly | Val |
|     | 50  |     |     |     |     | 55  |     |     |             |     | 60  |     |       |     |     |
| Gly | Thr | Gly | Ser | Ser | Ser | Leu | Trp | Asn | Leu         | Met | Gly | Asn | Ala   | Met | Val |
| 65  |     |     |     |     | 70  |     |     |     |             | 75  |     |     |       |     | 80  |
| Met | Thr | Gln | Tyr | Ile | Arg | Leu | Thr | Pro | Asp         | Met | Gln | Ser | Lys   | Gln | Gly |
|     |     |     |     | 85  |     |     |     |     | 90          |     |     |     |       | 95  |     |
| Ala | Leu | Trp | Asn | Arg | Val | Pro | Cys | Phe | Leu         | Arg | Asp | Trp | Glu   | Leu | Gln |
|     |     |     | 100 |     |     |     |     | 105 |             |     |     |     | 110   |     |     |
| Val | His | Phe | Lys | Ile | His | Gly | Gln | Gly | Lys         | Lys | Asn | Leu | His   | Gly | Asp |
|     |     | 115 |     |     |     |     | 120 |     |             |     |     | 125 |       |     |     |
| Gly | Leu | Ala | Ile | Trp | Tyr | Thr | Lys | Asp | Arg         | Met | Gln | Pro | Gly   | Pro | Val |
|     | 130 |     |     |     |     | 135 |     |     |             | -   | 140 |     |       |     |     |
| Phe | Gly | Asn | Met | Asp | Lys | Phe | Val | Gly | Leu         | Gly | Val | Phe | Val   | Asp | Thr |
| 145 |     |     |     |     | 150 |     |     |     |             | 155 |     |     |       |     | 160 |
| Tyr | Pro | Asn | Glu | Glu | Lys | Gln | Gln | Glu | Arg         | Val | Phe | Pro | Tyr   | Ile | Ser |
|     |     |     |     | 165 |     |     |     |     | 170         |     |     |     |       | 175 |     |
| Ala | Met | Val | Asn | Asn | Gly | Ser | Leu | Ser | Tyr         | Asp | His | Glu | Arg   | Asp | Gly |
|     |     |     | 180 | 1   |     |     |     | 185 | ;           |     |     |     | 190   |     |     |
| Arg | Pro | Thr | Glu | Leu | Gly | Gly | Cys | Thr | · Ala<br>سر | Ile | Val | Arg | , Asn | Leu | His |
|     |     | 195 | ,   |     |     |     | 200 | /   | -           |     |     | 205 | 5     |     |     |

Tyr Asp Thr Phe Leu Val Ile Arg Tyr Val Lys Arg His Leu Thr Ile Met Met Asp Ile Asp Gly Lys His Glu Trp Arg Asp Cys Ile Glu Val Pro Gly Val Arg Leu Pro Arg Gly Tyr Tyr Phe Gly Thr Ser Ser Ile Thr Gly Asp Leu Ser Asp Asn His Asp Val Ile Ser Leu Lys Leu Phe Glu Leu Thr Val Glu Arg Thr Pro Glu Glu Glu Lys Leu His Arg Asp Val Phe Leu Pro Ser Val Asp Asn Met Lys Leu Pro Glu Met Thr Ala Pro Leu Pro Pro Leu Ser Gly Leu Ala Leu Phe Leu Ile Val Phe Phe Ser Leu Val Phe Ser Val Phe Ala Ile Val Ile Gly Ile Ile Leu Tyr Asn Lys Trp Gln Glu Gln Ser Arg Lys Arg Phe Tyr 

<210> 63

<211> 261

<212> PRT

<213> Homo sapiens

<400> 63

Met Glu Leu Leu Gln Val Thr Ile Leu Phe Leu Leu Pro Ser Ile Cys

| 1   |     |     |     | 5   |     |            |     |     | 10      |     |     |     |     | 15  |     |
|-----|-----|-----|-----|-----|-----|------------|-----|-----|---------|-----|-----|-----|-----|-----|-----|
| Ser | Ser | Asn | Ser | Thr | Gly | Val        | Leu | Glu | Ala     | Ala | Asn | Asn | Ser | Leu | Val |
|     |     |     | 20  |     |     |            | •   | 25  |         |     |     |     | 30  |     |     |
| Val | Thr | Thr | Thr | Lys | Pro | Ser        | Ile | Thr | Thr     | Pro | Asn | Thr | Glu | Ser | Leu |
|     |     | 35  |     |     |     |            | 40  |     |         |     |     | 45  |     |     |     |
| Gln | Lys | Asn | Val | Val | Thr | Pro        | Thr | Thr | Gly     | Thr | Thr | Pro | Lys | Gly | Thr |
|     | 50  |     |     |     |     | <b>5</b> 5 |     |     |         |     | 60  |     |     |     |     |
| Ile | Thr | Asn | Glu | Leu | Leu | Lys        | Met | Ser | Leu     | Met | Ser | Thr | Ala | Thr | Phe |
| 65  |     |     |     |     | 70  |            |     |     |         | 75  |     |     |     |     | 80  |
| Leu | Thr | Ser | Lys | Asp | Glu | Gly        | Leu | Lys | Ala     | Thr | Thr | Thr | Asp | Val | Arg |
|     |     |     |     | 85  |     |            |     |     | 90      |     |     |     |     | 95  |     |
| Lys | Asn | Asp | Ser | Ile | Ile | Ser        | Asn | Val | Thr     | Val | Thr | Ser | Val | Thr | Leu |
|     |     |     | 100 |     |     |            |     | 105 |         |     |     |     | 110 |     |     |
| Pro | Asn | Ala | Val | Ser | Thr | Leu        | Gln | Ser | Ser     | Lys | Pro | Lys | Thr | Glu | Thr |
|     |     | 115 |     |     |     |            | 120 |     |         |     |     | 125 |     |     |     |
| G1n | Ser | Ser | Ile | Lys | Thr | Thr        | Glu | Ile | Pro     | Gly | Ser | Val | Leu | Gln | Pro |
|     | 130 |     |     |     |     | 135        |     |     |         |     | 140 |     |     |     |     |
| Asp | Ala | Ser | Pro | Ser | Lys | Thr        | G1y | Thr | Leu     | Thr | Ser | Ile | Pro | Val | Thr |
| 145 |     |     |     |     | 150 |            |     |     |         | 155 |     |     |     |     | 160 |
| Ile | Pro | Glu | Asn | Thr | Ser | Gln        | Ser | Gln | Val     | Ile | Gly | Thr | Glu | Gly | Gly |
|     |     |     |     | 165 |     |            |     |     | 170     |     |     |     |     | 175 |     |
| Lys | Asn | Ala | Ser | Thr | Ser | Ala        | Thr | Ser | Arg     | Ser | Tyr | Ser | Ser | Ile | Ile |
|     |     |     | 180 |     |     |            |     | 185 |         |     |     |     | 190 |     |     |
| Leu | Pro | Val | Val | Ile | Ala | Leu        | Ile | Val | Ile     | Thr | Leu | Ser | Val | Phe | Val |
|     |     | 195 |     |     |     |            | 200 | /   | ۰ تتمین |     |     | 205 |     |     |     |

| Leu  | اما       | GIY       | Leu       | Tyr | Arg | met              | cys              | ırp                     | Lys | АТА               | Asp              | Pro              | Gly              | Ihr        | Pro |
|------|-----------|-----------|-----------|-----|-----|------------------|------------------|-------------------------|-----|-------------------|------------------|------------------|------------------|------------|-----|
|      | 210       |           |           |     |     | 215              |                  |                         |     |                   | 220              |                  |                  |            |     |
| Glu  | Asn       | Gly       | Asn       | Asp | Gln | Pro              | Gln              | Ser                     | Asp | Lys               | Glu              | Ser              | Val              | Lys        | Leu |
| 225  |           |           |           |     | 230 |                  |                  |                         |     | 235               |                  |                  |                  |            | 240 |
| Leu  | Thr       | Val       | Lys       | Thr | Ile | Ser              | His              | Glu                     | Ser | Gly               | Glu              | His              | Ser              | Ala        | Gln |
|      |           |           |           | 245 |     |                  |                  |                         | 250 |                   |                  |                  |                  | 255        |     |
| Gly  | Lys       | Thr       | Lys       | Asn |     |                  |                  |                         |     |                   |                  |                  |                  |            |     |
|      |           |           | 260       |     |     |                  |                  |                         |     |                   |                  |                  |                  |            |     |
|      |           |           |           |     |     |                  |                  |                         |     |                   |                  |                  |                  |            |     |
| <210 | )> 64     | 1         |           |     |     |                  |                  |                         |     |                   |                  |                  |                  |            |     |
| <211 | l> 22     | 22        |           |     |     |                  |                  |                         |     |                   |                  |                  |                  |            |     |
| <212 | 2> PI     | TS        |           |     |     |                  |                  | •                       |     |                   |                  |                  |                  |            |     |
| <213 | 3> He     | omo :     | sapie     | ens |     |                  |                  |                         |     |                   |                  |                  |                  |            |     |
| <400 | )> 64     | 1         |           |     |     |                  |                  |                         |     |                   |                  |                  |                  |            |     |
| Met  | Leu       | Trp       | Leu       | Leu | Phe | Phe              | Leu              | Val                     | Thr | Ala               | Ile              | His              | Ala              | Glu        | Leu |
| 1    |           |           |           | 5   |     |                  |                  |                         | 10  |                   |                  |                  |                  | 15         |     |
| Cys  | Gln       | Pro       | Gly       | Ala | Glu | Asn              | Ala              | Pho                     | 1   | V - 1             | A                | I 411            | Ser              | Ile        | Arg |
|      |           |           |           |     |     |                  |                  | ı ne                    | Lys | vai               | AL. R            | Leu              |                  |            |     |
|      |           |           | 20        |     |     |                  |                  | 25                      | Lys | vai               | Arg              | Leu              | 30               |            |     |
| Thr  | Ala       | Leu       | 20<br>Gly | Asp | Lys |                  |                  | 25                      |     |                   |                  |                  | 30               |            | Tyr |
| Thr  | Ala       | Leu<br>35 |           | Asp | Lys |                  |                  | 25                      |     |                   |                  |                  | 30               |            | Tyr |
|      |           | 35        |           |     |     | Ala              | Tyr<br>40        | 25<br>Ala               | Trp | Asp               | Thr              | Asn<br>45        | 30<br>Glu        | Glu        |     |
|      |           | 35        | Gly       |     |     | Ala              | Tyr<br>40        | 25<br>Ala               | Trp | Asp               | Thr              | Asn<br>45        | 30<br>Glu        | Glu        |     |
| Leu  | Phe<br>50 | 35<br>Lys | Gly       | Met | Val | Ala<br>Ala<br>55 | Tyr<br>40<br>Phe | 25<br>Ala<br>Ser        | Trp | Asp<br>Arg        | Thr<br>Lys<br>60 | Asn<br>45<br>Val | 30<br>Glu<br>Pro | Glu<br>Asn | Arg |
| Leu  | Phe<br>50 | 35<br>Lys | Gly       | Met | Val | Ala<br>Ala<br>55 | Tyr<br>40<br>Phe | 25<br>Ala<br>Ser<br>Leu | Trp | Asp<br>Arg<br>Cys | Thr<br>Lys<br>60 | Asn<br>45<br>Val | 30<br>Glu<br>Pro | Glu<br>Asn | Arg |

WO 01/12660

#### 144/307

Pro Ala Val Glu Val Gln Ser Ala Ile Arg Met Asn Lys Asn Arg Ile Asn Asn Ala Phe Phe Leu Asn Asp Gln Thr Leu Glu Phe Leu Lys Ile Pro Ser Thr Leu Ala Pro Pro Met Asp Pro Ser Val Pro Ile Trp Ile Ile Ile Phe Gly Val Ile Phe Cys Ile Ile Ile Val Ala Ile Ala Leu Leu Ile Leu Ser Gly Ile Trp Gln Arg Arg Arg Lys Asn Lys Glu Pro Ser Glu Val Asp Asp Ala Glu Asp Lys Cys Glu Asn Met Ile Thr Ile Glu Asn Gly Ile Pro Ser Asp Pro Leu Asp Met Lys Gly Gly His Ile Asn Asp Ala Phe Met Thr Glu Asp Glu Arg Leu Thr Pro Leu

<210> 65

⟨211⟩ 183

<212> PRT

<213> Homo sapiens

<400> 65

Met Gly Val Arg Val His Val Val Ala Ala Ser Ala Leu Leu Tyr Phe

1 5 10 15

| Ile | Leu | Leu | Ser | Gly | Thr | Arg | Cys | Glu | Glu | Asn | Cys | Gly | Asn | Pro | Glu |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
|     |     |     | 20  | ,   |     |     |     | 25  |     |     |     |     | 30  |     |     |
| His | Cys | Leu | Thr | Thr | Asp | Trp | Val | His | Leu | Trp | Tyr | Ile | Trp | Leu | Leu |
|     |     | 35  |     |     |     |     | 40  |     |     |     |     | 45  |     |     |     |
| Val | Val | Ile | Gly | Ala | Leu | Leu | Leu | Leu | Cys | Gly | Leu | Thr | Ser | Leu | Cys |
|     | 50  |     |     |     |     | 55  |     |     |     |     | 60  |     |     |     |     |
| Phe | Arg | Cys | Cys | Cys | Leu | Ser | Arg | Gln | Gln | Asn | Gly | Glu | Asp | Gly | Gly |
| 65  |     |     |     |     | 70  |     |     |     |     | 75  |     |     |     |     | 80  |
| Pro | Pro | Pro | Cys | Glu | Val | Thr | Val | Ile | Ala | Phe | Asp | His | Asp | Ser | Thr |
|     |     |     |     | 85  |     |     |     |     | 90  |     |     |     |     | 95  |     |
| Leu | Gln | Ser | Thr | Ile | Thr | Ser | Leu | Gln | Ser | Val | Phe | Gly | Pro | Ala | Ala |
|     |     |     | 100 |     |     |     |     | 105 |     |     |     |     | 110 |     |     |
| Arg | Arg | Ile | Leu | Ala | Val | Ala | His | Ser | His | Ser | Ser | Leu | Gly | Gln | Leu |
|     |     | 115 |     |     |     |     | 120 |     |     |     |     | 125 |     |     |     |
| Pro | Ser | Ser | Leu | Asp | Thr | Leu | Pro | Gly | Tyr | Glu | Glu | Ala | Leu | His | Met |
|     | 130 |     |     |     |     | 135 |     |     |     |     | 140 |     |     |     |     |
| Ser | Arg | Phe | Thr | Val | Ala | Met | Cys | Gly | Gln | Lys | Ala | Pro | Asp | Leu | Pro |
| 145 |     |     |     |     | 150 |     |     |     |     | 155 |     |     |     |     | 160 |
| Pro | Val | Pro | Glu | Glu | Lys | Gln | Leu | Pro | Pro | Thr | Glu | Lys | Glu | Ser | Thr |
|     |     |     |     | 165 |     |     |     |     | 170 |     |     |     |     | 175 |     |
| Arg | Ile | Val | Asp | Ser | Trp | Asn |     |     |     |     |     |     |     |     |     |
|     |     |     | 180 |     |     |     |     |     |     |     |     |     |     |     |     |

⟨210⟩ 66

<211> 262

| <212 | > PR | T    |      |     |     |     |     |     |           |     |     |     |     |     |     |
|------|------|------|------|-----|-----|-----|-----|-----|-----------|-----|-----|-----|-----|-----|-----|
| <213 | > Ho | mo s | apie | ens |     |     |     |     |           |     |     |     |     |     |     |
| <400 | > 66 | ,    |      |     |     |     |     |     |           |     |     |     |     |     |     |
| Met  | Gly  | Lys  | Thr  | Phe | Ser | Gln | Leu | Gly | Ser       | Trp | Arg | Glu | Asp | Glu | Asn |
| 1    |      |      |      | 5   |     |     |     |     | 10        |     |     |     |     | 15  |     |
| Lys  | Ser  | Ile  | Leu  | Ser | Ser | Lys | Pro | Ala | Ile       | Gly | Ser | Lys | Ala | Val | Asn |
|      |      |      | 20   |     |     |     |     | 25  |           |     |     |     | 30  |     |     |
| Tyr  | Ser  | Ser  | Thr  | Gly | Ser | Ser | Lys | Ser | Phe       | Cys | Ser | Cys | Val | Pro | Cys |
|      |      | 35   |      |     |     |     | 40  |     |           |     |     | 45  |     |     |     |
| Glu  | Gly  | Thr  | Ala  | Asp | Ala | Ser | Phe | Val | Thr       | Cys | Pro | Thr | Cys | Gln | Gly |
|      | 50   |      |      |     |     | 55  |     |     |           |     | 60  |     |     |     |     |
| Ser  | Gly  | Lys  | Ile  | Pro | Gln | Glu | Leu | G1u | Lys       | Gln | Leu | Val | Ala | Leu | Ile |
| 65   |      |      |      |     | 70  |     |     |     |           | 75  |     |     |     |     | 80  |
| Pro  | Tyr  | Gly  | Asp  | Gln | Arg | Leu | Lys | Pro | Lys       | His | Thr | Lys | Leu | Phe | Val |
|      |      |      |      | 85  |     |     |     |     | 90        |     |     |     |     | 95  |     |
| Phe  | Leu  | Ala  | Val  | Leu | Ile | Cys | Leu | Val | Thr       | Ser | Ser | Phe | Ile | Val | Phe |
|      |      |      | 100  |     |     |     |     | 105 |           |     |     |     | 110 |     |     |
| Phe  | Leu  | Phe  | Pro  | Arg | Ser | Val | Ile | Val | Gln       | Pro | Ala | Gly | Leu | Asn | Ser |
|      |      | 115  |      |     |     |     | 120 |     |           |     |     | 125 |     |     |     |
| Ser  | Thr  | Val  | Ala  | Phe | Asp | Glu | Ala | Asp | Ile       | Tyr | Leu | Asn | Ile | Thr | Asn |
|      | 130  |      |      |     |     | 135 |     |     |           |     | 140 |     |     |     |     |
| Ile  | Leu  | Asn  | Ile  | Ser | Asn | Gly | Asn | Tyr | Tyr       | Pro | Ile | Met | Val | Thr | G1n |
| 145  |      |      |      |     | 150 | ı   |     |     |           | 155 | i   |     |     |     | 160 |
| Leu  | Thr  | Leu  | Glu  | Val | Leu | His | Leu | Ser | Leu       | Val | Val | Gly | Gln | Val | Ser |
|      |      |      |      | 165 | ;   |     |     | /   | ار<br>170 | )   |     |     |     | 175 | ;   |

| Asn           | Asn   | Leu   | Leu   | Leu | His | Ile | Gly | Pro | Leu  | Ala | Ser | Glu | Gln | Met | Phe |
|---------------|-------|-------|-------|-----|-----|-----|-----|-----|------|-----|-----|-----|-----|-----|-----|
|               |       |       | 180   |     |     |     |     | 185 |      |     |     |     | 190 |     |     |
| Tyr           | Ala   | Val   | Ala   | Thr | Lys | Ile | Arg | Asp | Glu  | Asn | Thr | Tyr | Lys | Ile | Cys |
|               |       | 195   |       |     |     |     | 200 |     |      |     |     | 205 |     |     |     |
| Thr           | Trp   | Leu   | Glu   | Ile | Lys | Val | His | His | Val  | Leu | Leu | His | Ile | Gln | Gly |
|               | 210   |       |       |     |     | 215 |     |     |      |     | 220 |     |     |     |     |
| Thr           | Leu   | Thr   | Cys   | Ser | Tyr | Leu | Ser | His | Ser  | Glu | Gln | Leu | Val | Phe | Gln |
| 225           |       |       |       |     | 230 |     |     |     |      | 235 |     |     |     |     | 240 |
| Ser           | Tyr   | Glu   | Tyr   | Val | Asp | Cys | Arg | Gly | Asn  | Ala | Ser | Val | Pro | His | G1n |
|               |       |       |       | 245 |     |     |     |     | 250  |     |     |     |     | 255 |     |
| Leu           | Thr   | Pro   | His   | Pro | Pro |     |     |     |      |     |     |     |     |     |     |
|               |       |       | 260   |     |     |     |     |     | ٠    |     |     |     |     |     | •   |
|               |       |       |       |     |     |     |     |     |      |     |     |     |     |     |     |
| <210          | 0> 67 | 7     |       |     |     |     |     |     |      |     |     |     |     |     |     |
| <b>&lt;21</b> | 1> 16 | 58    |       |     |     |     |     |     |      |     |     |     |     |     |     |
| <212          | 2> PI | TS    |       |     |     |     |     |     |      |     |     |     |     |     |     |
| <213          | 3> Ha | omo : | sapie | ens |     |     |     |     |      |     |     |     |     |     |     |
| <400          | 0> 67 | 7     |       |     |     |     |     |     |      |     |     |     |     |     |     |
| Met           | Gly   | Val   | Pro   | Thr | Ala | Leu | Glu | Ala | Gly  | Ser | Trp | Arg | Trp | Gly | Ser |
| 1             |       |       | •     | 5   |     |     |     |     | 10   |     |     |     |     | 15  |     |
| Leu           | Leu   | Phe   | Ala   | Leu | Phe | Leu | Ala | Ala | Ser  | Leu | Gly | Lys | Asp | Ala | Pro |
|               |       |       | 20    |     |     |     |     | 25  |      |     |     |     | 30  |     |     |
| Ser           | Asn   | Cys   | Val   | Val | Tyr | Pro | Ser | Ser | Ser  | Gln | Glu | Ser | Glu | Asn | Ile |
|               |       | 35    |       |     |     |     | 40  |     | المو |     |     | 45  |     |     |     |
| Thr           | Ala   | Ala   | Ala   | Leu | Ala | Thr | Gly | Ala | Cys  | Ile | Val | G1y | Ile | Leu | Cys |

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Leu Pro Leu Ile Leu Leu Leu Val Tyr Lys Gln Arg Gln Ala Ala Ser Asn Arg Arg Ala Gln Glu Leu Val Arg Met Asp Ser Asn Ile Gln Gly Ile Glu Asn Pro Gly Phe Glu Ala Ser Pro Pro Ala Gln Gly Ile Pro Glu Ala Lys Val Arg His Pro Leu Ser Tyr Val Ala Gln Arg Gln Pro Ser Glu Ser Gly Arg His Leu Leu Ser Glu Pro Ser Thr Pro Leu Ser Pro Pro Gly Pro Gly Asp Val Phe Phe Pro Ser Leu Asp Pro Val Pro Asp Ser Pro Asn Phe Glu Val Ile <210> 68 <211> 243 <212> PRT <213> Homo sapiens **<400>** 68 Met Ser Ser Gly Thr Glu Leu Leu Trp Pro Gly Ala Ala Leu Leu Val

20 25 30

Leu Leu Gly Val Ala Ala Ser Leu Cys Val Arg Cys Ser Arg Pro Gly

| Ala | Lys   | Arg   | Ser   | Glu   | Lys   | Ile   | Tyr   | Gln | Gln    | Arg   | Ser   | Leu   | Arg    | Glu   | Asp   |
|-----|-------|-------|-------|-------|-------|-------|-------|-----|--------|-------|-------|-------|--------|-------|-------|
|     |       | 35    |       |       |       |       | 40    |     |        |       |       | 45    |        |       |       |
| Gln | Gln   | Ser   | Phe   | Thr   | Gly   | Ser   | Arg   | Thr | Tyr    | Ser   | Leu   | Val   | Gly    | Gln   | Ala   |
|     | 50    |       |       |       |       | 55    |       |     |        |       | 60    |       |        |       |       |
| Trp | Pro   | Gly   | Pro   | Leu   | Ala   | Asp   | Met   | Ala | Pro    | Thr   | Arg   | Lys   | Asp    | Lys   | Leu   |
| 65  |       |       |       |       | 70    |       |       |     |        | 75    |       |       |        |       | 80    |
| Leu | Gln   | Phe   | Tyr   | Pro   | Ser   | Leu   | Glu   | Asp | Pro    | Ala   | Ser   | Ser   | Arg    | Tyr   | Gln   |
|     |       |       |       | 85    |       |       |       |     | 90     |       |       |       |        | 95    |       |
| Asn | Phe   | Ser   | Lys   | Gly   | Ser   | Arg   | His   | Gly | Ser    | Glu   | Glu   | Ala   | Tyr    | Ile   | Asp   |
|     |       |       | 100   |       |       |       |       | 105 |        |       |       |       | 110    |       |       |
| Pro | Ile   | Ala   | Met   | Glu   | Tyr   | Tyr   | Asn   | Trp | Gly    | Arg   | Phe   | Ser   | Lys    | Pro   | Pro   |
|     |       | 115   |       |       |       |       | 120   |     |        |       |       | 125   |        |       |       |
| Glu | Asp   | Asp   | Asp   | Ala   | Asn   | Ser   | Tyr   | Glu | Asn    | Val   | Leu   | Ile   | Cys    | Lys   | Gln   |
|     | 130   |       |       |       |       | 135   |       |     |        |       | 140   |       |        |       |       |
| Lys | Thr   | Thr   | Glu   | Thr   | Gly   | Ala   | Gln   | Gln | Glu    | Gly   | Ile   | Gly   | Gly    | Leu   | Cys   |
| 145 |       |       |       |       | 150   |       |       |     |        | 155   |       |       |        |       | 160   |
| Arg | G1y   | Asp   | Leu   | Ser   | Leu   | Ser   | Leu   | Ala | Leu    | Lys   | Thr   | Gly   | Pro    | Thr   | Ser   |
|     |       |       |       | 165   |       |       |       |     | 170    |       |       |       |        | 175   |       |
| Gly | Leu   | Cys   | Pro   | Ser   | Ala   | Ser   | Pro   | Glu | Glu    | Asp   | Glu   | G1u   | Ser    | Glu   | Asp   |
|     |       |       | 180   | )     |       |       |       | 185 | ·<br>• |       |       |       | 190    | )     |       |
| Tyr | Glr   | n Asr | ı Sei | . Ala | s Ser | · Ile | His   | G1n | Trp    | Arg   | Glu   | ı Ser | Arg    | Lys   | Val   |
|     |       | 198   | 5     |       |       |       | 200   | )   |        |       |       | 205   | 5      |       |       |
| Met | c Gly | , Glı | n Lei | ı Glı | n Are | g Glu | ı Ala | Ser | Pro    | G13   | r Pro | Val   | l Gly  | 7 Ser | Pro   |
|     | 210   | )     |       |       |       | 215   | 5     |     | ۰ نثرو |       | 220   | )     |        |       |       |
| Acı | s Gli | ı Clı | n Ası | n G1: | v Gli | ı Pro | n Asr | Yvı | - Val  | l Ası | n G1v | v G1: | ı ·Va` | l Als | . Ala |

225 230 235 240 Thr Glu Ala <210> 69 <211> 428 <212> PRT <213> Homo sapiens <400> 69 Met Ala Arg Ser Leu Cys Pro Gly Ala Trp Leu Arg Lys Pro Tyr Tyr 5 1 10 15 Leu Gln Ala Arg Phe Ser Tyr Val Arg Met Lys Tyr Leu Phe Phe Ser 20 25 30 Trp Leu Val Val Phe Val Gly Ser Trp Ile Ile Tyr Val Gln Tyr Ser 35 40 45 Thr Tyr Thr Glu Leu Cys Arg Gly Lys Asp Cys Lys Lys Ile Ile Cys 50 55 60 Asp Lys Tyr Lys Thr Gly Val Ile Asp Gly Pro Ala Cys Asn Ser Leu 70 65 75 80 Cys Val Thr Glu Thr Leu Tyr Phe Gly Lys Cys Leu Ser Thr Lys Pro 85 90 95 Asn Asn Gln Met Tyr Leu Gly Ile Trp Asp Asn Leu Pro Gly Val Val 100 105 110

115 120 / 125

Lys Cys Gln Met Glu Gln Ala Leu His Leu Asp Phe Gly Thr Glu Leu

| Glu | Pro | Arg | Lys | Glu | Ile | Val | Leu | Phe | Asp    | Lys | Pro | Thr | Arg | Gly | Thr |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|--------|-----|-----|-----|-----|-----|-----|
|     | 130 |     |     |     |     | 135 |     |     |        |     | 140 |     |     |     |     |
| Thr | Val | Gln | Lys | Phe | Lys | Glu | Met | Val | Tyr    | Ser | Leu | Phe | Lys | Ala | Lys |
| 145 |     |     |     |     | 150 |     |     |     |        | 155 |     |     |     |     | 160 |
| Leu | Gly | Asp | Gln | Gly | Asn | Leu | Ser | Glu | Leu    | Val | Asn | Leu | Ile | Leu | Thr |
|     |     |     |     | 165 |     |     |     |     | 170    |     |     |     |     | 175 |     |
| Val | Ala | Asp | G1y | Asp | Lys | Asp | Gly | Gln | Val    | Ser | Leu | Gly | Glu | Ala | Lys |
|     |     |     | 180 |     |     |     |     | 185 |        |     |     |     | 190 |     |     |
| Ser | Ala | Trp | Ala | Leu | Leu | G1n | Leu | Asn | Glu    | Phe | Leu | Leu | Met | Val | Ile |
|     |     | 195 |     |     |     |     | 200 |     |        |     |     | 205 |     |     |     |
| Leu | Gln | Asp | Lys | Glu | His | Thr | Pro | Lys | Leu    | Met | Gly | Phe | Cys | Gly | Asp |
|     | 210 |     | ,   |     |     | 215 |     |     |        |     | 220 |     |     |     |     |
| Leu | Tyr | Val | Met | Glu | Ser | Val | Glu | Tyr | Thr    | Ser | Leu | Tyr | Gly | Ile | Ser |
| 225 |     |     |     |     | 230 |     |     |     |        | 235 |     |     |     |     | 240 |
| Leu | Pro | Trp | Val | Ile | Glu | Leu | Phe | Ile | Pro    | Ser | Gly | Phe | Arg | Arg | Ser |
|     |     |     |     | 245 |     |     |     |     | 250    |     |     |     |     | 255 |     |
| Met | Asp | Gln | Leu | Phe | Thr | Pro | Ser | Trp | Pro    | Arg | Lys | Ala | Lys | Ile | Ala |
|     |     |     | 260 |     |     |     |     | 265 |        |     |     |     | 270 |     |     |
| Ile | Gly | Leu | Leu | Glu | Phe | Val | Glu | Asp | Val    | Phe | His | Gly | Pro | Tyr | Gly |
|     |     | 275 |     |     |     |     | 280 |     |        |     |     | 285 |     |     |     |
| Asn | Phe | Leu | Met | Cys | Asp | Thr | Ser | Ala | Lys    | Asn | Leu | Gly | Tyr | Asn | Asp |
|     | 290 |     |     |     |     | 295 |     |     |        |     | 300 |     |     |     |     |
| Lys | Tyr | Asp | Leu | Lys | Met | Val | Asp | Met | Arg    | Lys | Ile | Val | Pro | Glu | Thr |
| 305 |     |     |     |     | 310 |     |     |     | ۰ تغیق | 315 |     |     |     |     | 320 |
| Asn | Leu | Lys | Glu | Leu | Ile | Lys | Asp | Arg | His    | Cys | Glu | Ser | Asp | Leu | Asp |

Cys Val Tyr Gly Thr Asp Cys Arg Thr Ser Cys Asp Gln Ser Thr Met Lys Cys Thr Ser Glu Val Ile Gln Pro Asn Leu Ala Lys Ala Cys Gln Leu Leu Lys Asp Tyr Leu Leu Arg Gly Ala Pro Ser Glu Ile Arg Glu Glu Leu Glu Lys Gln Leu Tyr Ser Cys Ile Ala Leu Lys Val Thr Ala Asn Gln Met Glu Met Glu His Ser Leu Ile Leu Asn Asn Leu Lys Thr Leu Leu Trp Lys Lys Ile Ser Tyr Thr Asn Asp Ser <210> 70 <211> 283 <212> PRT <213> Homo sapiens <400> 70 Met Pro His Ser Ser Leu His Pro Ser Ile Pro Cys Pro Arg Gly His Gly Ala Gln Lys Ala Ala Leu Val Leu Leu Ser Ala Cys Leu Val Thr Leu Trp Gly Leu Gly Glu Pro Pro Glu His Thr Leu Arg Tyr Leu Val 

| Leu | His | Leu | Ala | Ser | Leu | Gln | Leu | Gly  | Leu       | Leu              | Leu | Asn | Gly | Val | Cys |
|-----|-----|-----|-----|-----|-----|-----|-----|------|-----------|------------------|-----|-----|-----|-----|-----|
|     | 50  |     |     |     |     | 55  |     |      |           |                  | 60  |     |     |     |     |
| Ser | Leu | Ala | Glu | Glu | Leu | His | His | Ile  | His       | Ser              | Arg | Tyr | Arg | Gly | Ser |
| 65  |     |     |     |     | 70  |     |     |      |           | 75               |     |     |     |     | 80  |
| Tyr | Trp | Arg | Thr | Val | Arg | Ala | Cys | Leu  | Gly       | Cys              | Pro | Leu | Arg | Arg | Gly |
|     |     |     |     | 85  |     |     |     |      | 90        |                  |     |     |     | 95  |     |
| Ala | Leu | Leu | Leu | Leu | Ser | Ile | Tyr | Phe  | Tyr       | Tyr              | Ser | Leu | Pro | Asn | Ala |
|     |     |     | 100 |     |     |     |     | 105  |           |                  |     |     | 110 |     |     |
| Val | Gly | Pro | Pro | Phe | Thr | Trp | Met | Leu  | Ala       | Leu              | Leu | Gly | Leu | Ser | Gln |
|     |     | 115 |     |     |     |     | 120 |      |           |                  |     | 125 |     |     |     |
| Ala | Leu | Asn | Ile | Leu | Leu | Gly | Leu | Lys  | Gly       | Leu              | Ala | Pro | Ala | Glu | Ile |
|     | 130 |     |     |     |     | 135 |     |      |           |                  | 140 |     |     |     |     |
| Ser | Ala | Val | Cys | Glu | Lys | Gly | Asn | Phe  | Asn       | Val              | Ala | His | Gly | Leu | Ala |
| 145 |     |     |     |     | 150 |     |     |      |           | 155              |     |     |     |     | 160 |
| Trp | Ser | Tyr | Tyr | Ile | Gly | Tyr | Leu | Arg  | Leu       | Ile              | Leu | Pro | Glu | Leu | G1n |
|     |     |     |     | 165 |     |     |     |      | 170       |                  |     |     |     | 175 |     |
| Ala | Arg | Ile | Arg | Thr | Tyr | Asn | Gln | His  | Tyr       | Asn              | Asn | Leu | Leu | Arg | Gly |
|     |     |     | 180 |     |     |     |     | 185  |           |                  |     |     | 190 |     |     |
| Ala | Val | Ser | Gln | Arg | Leu | Tyr | Ile | Leu  | Leu       | Pro              | Leu | Asp | Cys | Gly | Val |
|     |     | 195 |     |     |     |     | 200 |      |           |                  |     | 205 |     |     |     |
| Pro | Asp | Asn | Leu | Ser | Met | Ala | Asp | Pro  | Asn       | Ile              | Arg | Phe | Leu | Asp | Lys |
|     | 210 |     |     |     |     | 215 |     |      |           |                  | 220 |     |     |     |     |
| Leu | Pro | Gln | Gln | Thr | Ala | Asp | Arg | Ala  | Gly       | Ile              | Lys | Asp | Arg | Val | Tyr |
| 225 |     |     |     |     | 230 |     |     | ,    | ** بمشمين | 235              |     |     |     |     | 240 |
| Ser | Asn | Sor | Ile | Tur | Glu | Lau | Lau | cî., | Acr       | G1 <sub>22</sub> | Cl. | A   | ۸   | 1   | C1- |

245

250

255

Met Thr Ala Ala Ser Arg Cys Pro Arg Arg Phe Ser Gly Thr Cys Gly

260

265

270

Arg Arg Lys Arg Lys Arg Leu Leu Trp Ala Ala

275

280

⟨210⟩ 71

⟨211⟩ 1167

<212> DNA

<213> Homo sapiens

<400> 71

atggatagag gggagaaaat acagctcaag agagtgtttg gatattggtg gggcacaagt 60 120 tttttgctta ttaatatcat tggtgcagga atttttgtgt cccccaaagg tgtgttggca tactcttgca tgaacgtggg agtctccctg tgcgtttggg ctggctgtgc catactggcc 180 240 atgacatcaa ctctttgctc tgcagagata agtataagct tcccatgcag tggagctcaa 300 tactattttc tcaagagata ctttggctcc acggttgctt ttttgaatct ctggacatcc 360 ttgtttctgg ggtcaggggt agttgctggc caagctctgc tccttgctga gtacagcatc 420 cagcettttt ttcccagetg ctctgtccca aagetgccta agaaatgtct ggcattggcc 480 atgttgtgga ttgtaggaat tctgacttct cgtggtgtga aagaagtgac ttggcttcag 540 atagctaget cagtgetgaa agtgteeata ettagettea ttteeetaac tggagtagtg 600 ttcctgataa gagggaaaaa ggagaatgta gaacgatttc agaatgcttt tgatgctgaa 660 cttccagata tctctcacct tatacaagcc atcttccaag gatattttgc atattcaggg 720 gagctgaaga agcccagaac aacaattccc aaatgcatat ttactgcgtt acctctggtg 780 actgtagttt atttactggt taacatttcc tatctgactg ttctgacacc cagggaaatt ctctcttcag atgctgtagc tatcacatgg gctgatcgag cttttccctc attagcatgg 840

| attatgcctt | ttgctatttc | tacctcatta | tttagcaacc | ttctgatttc | tatatttaaa | 900  |
|------------|------------|------------|------------|------------|------------|------|
| tcttcgagac | caatatatct | tgcaagccaa | gagggccagc | tgcctttgct | atttaataca | 960  |
| cttaatagtc | actettetee | atttacagct | gtgctactac | ttgtcacttt | gggatccctt | 1020 |
| gcaattatct | taacaagtct | aattgatttg | ataaactata | ttttttcac  | gggttcatta | 1080 |
| tggtctatat | tattaatgat | aggaatacta | aggcggagat | accaggaacc | caatctatct | 1140 |
| ataccttata | aggtaaaatt | ggatttc    |            |            |            | 1167 |

⟨210⟩ 72

⟨211⟩ 1044

<212> DNA

<213> Homo sapiens

<400> 72

atggcggcga ctctgggacc ccttgggtcg tggcagcagt ggcggcgatg tttgtcggct 60 cgggatgggt ccaggatgtt actccttctt cttttgttgg ggtctgggca ggggccacag 120 caagtcgggg cgggtcaaac gttcgagtac ttgaaacggg agcactcgct gtcgaagccc 180 taccagggtg tgggcacagg cagttcctca ctgtggaatc tgatgggcaa tgccatggtg 240 atgacccagt atatccgcct taccccagat atgcaaagta aacagggtgc cttgtggaac 300 cgggtgccat gtttcctgag agactgggag ttgcaggtgc acttcaaaat ccatggacaa 360 ggaaagaaga atctgcatgg ggatggcttg gcaatctggt acacaaagga tcggatgcag 420 ccagggcctg tgtttggaaa catggacaaa tttgtggggc tgggagtatt tgtagacacc 480 taccccaatg aggagaagca gcaagagcgg gtattcccct acatctcagc catggtgaac 540 aacggctccc tcagctatga tcatgagcgg gatgggcggc ctacagagct gggaggctgc 600 acagccattg tecgeaatet teattacgae acetteetgg tgattegeta egteaagagg 660 catttgacga taatgatgga tattgatggc aagcatgagt ggagggactg cattgaagtg 720 cccggagtcc gcctgccccg cggctactac ttcggcacct cctccatcac tggggatctc 780

| tcagataatc | atgatgtcat | ttccttgaag | ttgtttgaac | tgacagtgga | gagaacccca | 840  |
|------------|------------|------------|------------|------------|------------|------|
| gaagaggaaa | agctccatcg | agatgtgttc | ttgccctcag | tggacaatat | gaagctgcct | 900  |
| gagatgacag | ctccactgcc | gcccctgagt | ggcctggccc | tcttcctcat | cgtcttttc  | 960  |
| tccctggtgt | tttctgtatt | tgccatagtc | attggtatca | tactctacaa | caaatggcag | 1020 |
| gaacagagcc | gaaagcgctt | ctac .     |            |            |            | 1044 |

<210> 73

<211> 783

<212> DNA

<213> Homo sapiens

<400> 73

atggaactgc ttcaagtgac cattetttt ettetgeeca gtatttgeag cagtaacage 60 acaggigtit tagaggcagc taataattca citgitgita ciacaacaaa accatciata 120 acaacaccaa acacagaatc attacagaaa aatgttgtca caccaacaac tggaacaact 180 cctaaaggaa caatcaccaa tgaattactt aaaatgtctc tgatgtcaac agctactttt 240 ttaacaagta aagatgaagg attgaaagcc acaaccactg atgtcaggaa gaatgactcc 300 atcatttcaa acgtaacagt aacaagtgtt acacttccaa atgctgtttc aacattacaa 360 agttccaaac ccaagactga aactcagagt tcaattaaaa caacagaaat accaggtagt 420 gttctacaac cagatgcatc accttctaaa actggtacat taacctcaat accagttaca 480 attccagaaa acacctcaca gtctcaagta ataggcactg agggtggaaa aaatgcaagc 540 acttcagcaa ccagccggtc ttattccagt attattttgc cggtggttat tgctttgatt 600 gtaataacac tttcagtatt tgttctggtg ggtttgtacc gaatgtgctg gaaggcagat 660 ccgggcacac cagaaaatgg aaatgatcaa cctcagtctg ataaagagag cgtgaagctt 720 cttaccgtta agacaatttc tcatgagtct ggtgagcact ctgcacaagg aaaaaccaag 780 aac 783

| <210> | 74  |
|-------|-----|
| <211> | 666 |
| <212> | DNA |

<213> Homo sapiens

⟨400⟩ 74

| atgttgtggc | tgctcttttt | tctggtgact | gccattcatg | ctgaactctg. | tcaaccaggt | 60  |
|------------|------------|------------|------------|-------------|------------|-----|
| gcagaaaatg | cttttaaagt | gagacttagt | atcagaacag | ctctgggaga  | taaagcatat | 120 |
| gcctgggata | ccaatgaaga | atacctcttc | aaagcgatgg | tagctttctc  | catgagaaaa | 180 |
| gttcccaaca | gagaagcaac | agaaatttcc | catgtcctac | tttgcaatgt  | aacccagagg | 240 |
| gtatcattct | ggtttgtggt | tacagaccct | tcaaaaaatc | acacccttcc  | tgctgttgag | 300 |
| gtgcaatcag | ccataagaat | gaacaagaac | cggatcaaca | atgccttctt  | tctaaatgac | 360 |
| caaactctgg | aattttaaa  | aatcccttcc | acacttgcac | cacccatgga  | cccatctgtg | 420 |
| cccatctgga | ttattatatt | tggtgtgata | ttttgcatca | tcatagttgc  | aattgcacta | 480 |
| ctgattttat | cagggatctg | gcaacgtaga | agaaagaaca | aagaaccatc  | tgaagtggat | 540 |
| gacgctgaag | ataagtgtga | aaacatgatc | acaattgaaa | atggcatccc  | ctctgatccc | 600 |
| ctggacatga | agggagggca | tattaatgat | gccttcatga | cagaggatga  | gaggctcacc | 660 |
| cctctc     |            |            |            |             |            | 666 |

⟨210⟩ 75

⟨211⟩ 549

<212> DNA

<213> Homo sapiens

⟨400⟩ 75

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#### 158/307

| gggacgagat | gtgaggaaaa | ctgtggtaat | cctgaacatt | gcctgaccac | agactgggta | 120 |
|------------|------------|------------|------------|------------|------------|-----|
| catctctggt | atatatggtt | gctagtggta | attggcgcgc | tgcttctcct | gtgtggcctg | 180 |
| acgtccctgt | gcttccgctg | ctgctgtctg | agccgccagc | aaaatgggga | agatgggggc | 240 |
| ccaccaccct | gtgaagtgac | cgtcattgct | ttcgatcacg | acagcactct | ccagagcact | 300 |
| atcacatctc | tgcagtcggt | gtttggccct | gcagctcgga | ggatcctggc | tgtggctcac | 360 |
| tcccacagct | ccctgggcca | getgeeetee | tctttggaca | ccctcccagg | gtatgaagaa | 420 |
| gctcttcaca | tgagtcgctt | cacagtagcc | atgtgcgggc | agaaagcacc | tgatctaccc | 480 |
| ccagtacctg | aagaaaagca | gctgcctcca | acagagaagg | agtcgactcg | aatagttgac | 540 |
| tcttggaac  |            |            |            |            |            | 549 |

<210> 76

<211> 786

<212> DNA

<213> Homo sapiens

<400> 76

60 atgggtaaga cgttttccca gctgggctct tggcgggagg atgagaacaa gtcaatcctg tcctccaaac cagccattgg cagcaaggct gtcaactact ccagcaccgg tagcagcaag 120 180 tcttttgtt cctgtgtgcc ttgtgaagga actgctgatg ccagcttcgt gacttgtccc 240 acctgccagg gcagtggcaa gattccccaa gagctggaga agcagttggt ggctctcatt 300 ccctatgggg accagaggct gaagcccaag cacacgaagc tctttgtgtt cctggccgtg 360 ctcatctgcc tggtgacctc ctccttcatc gtctttttcc tgtttccccg gtccgtcatt 420 gtgcagcctg caggcctcaa ctcctccaca gtggcctttg atgaggctga tatctacctc 480 aacataacga atatcttaaa catctccaat ggcaactact accccattat ggtgacacag 540 ctgaccetcg aggttetgea cetgteete gtggtggge aggttteeaa caacettete 600 ctacacattg gccctttggc cagtgaacag atgttttacg cagtagctac caagatacgg

| gatgaaaaca | catacaaaat | ctgtacctgg | ctggaaatca | aagtccacca | tgtgcttttg | 660 |
|------------|------------|------------|------------|------------|------------|-----|
| cacatccagg | gcaccctgac | ctgttcatac | ctgagccatt | cagagcagct | ggtctttcag | 720 |
| agctatgaat | atgtggactg | ccgaggaaac | gcatctgtgc | cccaccagct | gacccctcac | 780 |
| ccacca     |            |            |            |            |            | 786 |
|            |            |            |            |            |            |     |
| <210> 77   |            |            |            |            |            |     |
| <211> 504  |            |            |            |            |            |     |
| <212> DNA  |            |            |            |            |            |     |
| <213> Homo | sapiens    |            |            |            |            |     |
| <400> 77   |            |            |            |            |            |     |
| atgggcgtcc | ccacggccct | ggaggccggc | agctggcgct | ggggatccct | gctcttcgct | 60  |
| ctcttcctgg | ctgcgtccct | aggcaaagat | gcaccatcca | actgtgtggt | gtacccatcc | 120 |
| tcctcccagg | agagtgaaaa | catcacggct | gcagccctgg | ctacgggtgc | ctgcatcgta | 180 |
| ggaatcctct | gcctcccct  | catcctgctc | ctggtctaca | agcaaaggca | ggcagcctcc | 240 |
| aaccgccgtg | cccaggagct | ggtgcggatg | gacagcaaca | ttcaagggat | tgaaaacccc | 300 |
| ggctttgaag | cctcaccacc | tgcccagggg | atacccgagg | ccaaagtcag | gcaccccctg | 360 |
| tcctatgtgg | cccagcggca | gccttctgag | tctgggcggc | atctgctttc | ggagcccagc | 420 |
| accccctgt  | ctcctccagg | ccccggagac | gtcttcttcc | catccctgga | ccctgtccct | 480 |
| gactctccaa | actttgaggt | catc       |            |            |            | 504 |
|            |            |            |            |            |            |     |

⟨210⟩ 78

<211> 729

<212> DNA

<213> Homo sapiens

⟨400⟩ 78

| atgagctcgg | ggactgaact | gctgtggccc | ggagcagcgc | tgctggtgct | gttgggggtg | 60  |
|------------|------------|------------|------------|------------|------------|-----|
| gcagccagtc | tgtgtgtgcg | ctgctcacgc | ccaggtgcaa | agaggtcaga | gaaaatctac | 120 |
| cagcagagaa | gtctgcgtga | ggaccaacag | agctttacgg | ggtcccggac | ctactccttg | 180 |
| gtcgggcagg | catggccagg | acccctggcg | gacatggcac | ccacaaggaa | ggacaagctg | 240 |
| ttgcaattct | accccagcct | ggaggatcca | gcatcttcca | ggtaccagaa | cttcagcaaa | 300 |
| ggaagcagac | acgggtcgga | ggaagcctac | atagacccca | ttgccatgga | gtattacaac | 360 |
| tgggggcggt | tctcgaagcc | cccagaagat | gatgatgcca | attcctacga | gaatgtgctc | 420 |
| atttgcaagc | agaaaaccac | agagacaggt | gcccagcagg | agggcatagg | tggcctctgc | 480 |
| agaggggacc | tcagcctgtc | actggccctg | aagactggcc | ccacttctgg | tctctgtccc | 540 |
| tctgcctccc | cggaagaaga | tgaggaatct | gaggattatc | agaactcagc | atccatccat | 600 |
| cagtggcgcg | agtccaggaa | ggtcatgggg | caactccaga | gagaagcatc | ccctggcccg | 660 |
| gtgggaagcc | cagacgagga | ggacggggaa | ccggattacg | tgaatgggga | ggtggcagcc | 720 |
| acagaagcc  |            |            |            |            |            | 729 |

<210> 79

<211> 1284

<212> DNA

<213≻ Homo sapiens

<400> 79

atggcgagga gtctctgtcc gggggcctgg ctaaggaaac cctattacct ccaggctcgc 60

ttctcatatg tgcggatgaa atatctttc ttttcctggt tagtggtttt tgttggaagc 120

tggattatat atgtgcagta ttctacctat acagaattat gcagaggaaa ggactgtaag 180

aaaataatat gtgacaagta caagactgga gttattgatg ggcctgcatg taacagcctt 240

tgtgttacag aaactcttta ctttggaaaa tgtttatcca ccaagcccaa caatcagatg 300

tatttaggga tttgggataa tctaccaggt gttgtgaaat gtcaaatgga acaagcgctt 360

| catcttgatt | ttggaactga | attggaacca | agaaaagaaa | tagtgctatt | tgataagcca | 420  |
|------------|------------|------------|------------|------------|------------|------|
| actagaggaa | ctactgtaca | aaaatttaaa | gaaatggtct | atagtctctt | taaggcaaaa | 480  |
| ttgggtgacc | aaggaaacct | ctctgaactg | gttaatctca | tcttgacggt | ggctgatgga | 540  |
| gacaaagatg | gccaggtttc | cttgggagaa | gcaaagtcgg | catgggcact | tcttcaactg | 600  |
| aatgaatttc | ttctcatggt | gatacttcaa | gataaagaac | atacccccaa | attaatggga | 660  |
| ttctgtggtg | acctctatgt | gatggaaagt | gttgaatata | cctctcttta | tggaataagc | 720  |
| cttccttggg | tcattgaact | ttttattcca | tctgggttca | gaagaagcat | ggatcagctg | 780  |
| ttcacaccat | catggccaag | aaaggccaaa | atagccatag | gacttctaga | atttgtggaa | 840  |
| gatgttttcc | atggccccta | cggaaatttc | ctcatgtgcg | atactagtgc | caaaaaccta | 900  |
| ggatataatg | ataagtatga | tttgaaaatg | gtggatatga | gaaaaattgt | gccagagaca | 960  |
| aacctgaaag | aacttattaa | ggatcgtcac | tgtgagtctg | atttggactg | tgtctatggc | 1020 |
| acagattgta | gaactagctg | tgatcagagt | acaatgaagt | gtacttcaga | agtgatacaa | 1080 |
| ccaaacttgg | caaaagcttg | tcagttactc | aaagactacc | tactgcgtgg | tgctccaagt | 1140 |
| gaaattcgtg | aagaattaga | aaagcagctt | tattcttgta | ttgctctcaa | agtcacagca | 1200 |
| aatcaaatgg | aaatggaaca | ttctttgata | ctaaataacc | taaaaacatt | attgtggaag | 1260 |
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| aacggggtct | gcagcctggc | tgaggagctg | caccacatcc | actccaggta | ccggggcagc | 240 |
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| tactggagga | ctgtgcgggc | ctgcctgggc | tgcccctcc  | gccgtggggc | cctgttgctg | 300 |
| ctgtccatct | atttctacta | ctccctccca | aatgcggtcg | gcccgccctt | cacttggatg | 360 |
| cttgccctcc | tgggcctctc | gcaggcactg | aacatcctcc | tgggcctcaa | gggcctggcc | 420 |
| ccagctgaga | tctctgcagt | gtgtgaaaaa | gggaatttca | acgtggccca | tgggctggca | 480 |
| tggtcatatt | acatcggata | tctgcggctg | atcctgccag | agctccaggc | ccggattcga | 540 |
| acttacaatc | agcattacaa | caacctgcta | cggggtgcag | tgagccagcg | gctgtatatt | 600 |
| ctcctcccat | tggactgtgg | ggtgcctgat | aacctgagta | tggctgaccc | caacattcgc | 660 |
| ttcctggata | aactgcccca | gcagaccgct | gaccgtgctg | gcatcaagga | tcgggtttac | 720 |
| agcaacagca | tctatgagct | tctggagaac | gggcagcgga | acctgcagat | gacagcagct | 780 |
| tctcgctgtc | ccaggaggtt | ctccggcacc | tgcggcagga | ggaaaaggaa | gaggttactg | 840 |
| tgggcagct  |            |            |            |            | •          | 849 |

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Met Asp Arg Gly Glu

| aaa | ata | cag | ctc | aag | aga | gtg | ttt | gga | tat      | tgg | tgg | ggc | aca | agt | ttt | 162 |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|----------|-----|-----|-----|-----|-----|-----|-----|
| Lys | Ile | Gln | Leu | Lys | Arg | Val | Phe | Gly | Tyr      | Trp | Trp | Gly | Thr | Ser | Phe |     |
|     |     |     |     | 10  |     |     |     |     | 15       |     |     |     |     | 20  |     |     |
| ttg | ctt | att | aat | atc | att | ggt | gca | gga | att      | ttt | gtg | tcc | ccc | aaa | ggt | 210 |
| Leu | Leu | Ile | Asn | Ile | Ile | Gly | Ala | Gly | Ile      | Phe | Val | Ser | Pro | Lys | Gly |     |
|     |     |     | 25  |     |     |     |     | 30  |          |     |     |     | 35  |     |     |     |
| gtg | ttg | gca | tac | tct | tgc | atg | aac | gtg | gga      | gtc | tcc | ctg | tgc | gtt | tgg | 258 |
| Val | Leu | Ala | Tyr | Ser | Cys | Met | Asn | Val | Gly      | Val | Ser | Leu | Cys | Val | Trp |     |
|     |     | 40  |     |     |     |     | 45  |     |          |     |     | 50  |     |     |     |     |
| gct | ggc | tgt | gcc | ata | ctg | gcc | atg | aca | tca      | act | ctt | tgc | tct | gca | gag | 306 |
| Ala | Gly | Cys | Ala | Ile | Leu | Ala | Met | Thr | Ser      | Thr | Leu | Cys | Ser | Ala | Glu |     |
| .*  | 55  |     |     |     |     | 60  |     |     |          |     | 65  |     | -   |     |     |     |
| ata | agt | ata | agc | ttc | cca | tgc | agt | gga | gct      | caa | tac | tat | ttt | ctc | aag | 354 |
| Ile | Ser | Ile | Ser | Phe | Pro | Cys | Ser | Gly | Ala      | Gln | Tyr | Tyr | Phe | Leu | Lys |     |
| 70  |     |     |     |     | 75  |     |     |     |          | 80  |     |     |     |     | 85  |     |
| aga | tac | ttt | ggc | tcc | acg | gtt | gct | ttt | ttg      | aat | ctc | tgg | aca | tcc | ttg | 402 |
| Arg | Tyr | Phe | Gly | Ser | Thr | Val | Ala | Phe | Leu      | Asn | Leu | Trp | Thr | Ser | Leu |     |
|     |     |     |     | 90  |     |     |     |     | 95       |     |     |     |     | 100 |     |     |
| ttt | ctg | ggg | tca | ggg | gta | gtt | gct | ggc | caa      | gct | ctg | ctc | ctt | gct | gag | 450 |
| Phe | Leu | Gly | Ser | Gly | Val | Val | Ala | Gly | Gln      | Ala | Leu | Leu | Leu | Ala | Glu |     |
|     |     |     | 105 |     |     |     |     | 110 | -        |     |     | •   | 115 |     |     |     |
| tac | agc | atc | cag | cct | ttt | ttt | ccc | agc | tgc      | tct | gtc | cca | aag | ctg | cct | 498 |
| Tyr | Ser | Ile | Gln | Pro | Phe | Phe | Pro | Ser | Cys      | Ser | Val | Pro | Lys | Leu | Pro |     |
|     |     | 120 |     |     |     |     | 125 |     | التاعتنس |     |     | 130 |     |     |     |     |
| aag | aaa | tgt | ctg | gca | ttg | gcc | atg | ttg | tgg      | att | gta | gga | att | ctg | act | 546 |

WO 01/12660 PCT/JP00/05356

| Lys | Lys | Cys   | Leu   | Ala   | Leu  | Ala | Met   | Leu   | Trp         | Ile | Val | Gly   | Ile | Leu | Thr   |     |
|-----|-----|-------|-------|-------|------|-----|-------|-------|-------------|-----|-----|-------|-----|-----|-------|-----|
|     | 135 |       |       |       |      | 140 |       |       |             |     | 145 |       |     |     |       |     |
| tct | cgt | ggt   | gtg   | aaa   | gaa  | gtg | act   | tgg   | ctt         | cag | ata | gct   | agc | tca | gtg   | 594 |
| Ser | Arg | Gly   | Val   | Lys   | Glu  | Val | Thr   | Trp   | Leu         | Gln | Ile | Ala   | Ser | Ser | Val   |     |
| 150 |     |       |       |       | 155  |     |       |       |             | 160 |     |       |     |     | 165   |     |
| ctg | aaa | gtg   | tcc   | ata   | ctt  | agc | ttc   | att   | tcc         | cta | act | gga   | gta | gtg | ttc   | 642 |
| Leu | Lys | Val   | Ser   | Ile   | Leu  | Ser | Phe   | Ile   | Ser         | Leu | Thr | Gly   | Val | Val | Phe   |     |
|     |     |       |       | 170   |      |     |       |       | 175         |     |     |       |     | 180 |       |     |
| ctg | ata | aga   | ggg   | aaa   | aag  | gag | aat   | gta   | gaa         | cga | ttt | cag   | aat | gct | ttt   | 690 |
| Leu | Ile | Arg   | Gly   | Lys   | Lys  | Glu | Asn   | Val   | Glu         | Arg | Phe | Gln   | Asn | Ala | Phe   |     |
|     |     |       | 185   |       |      |     |       | 190   |             |     |     |       | 195 |     |       |     |
| gat | gct | gaa   | ctt   | cca   | gat  | atc | tct   | cac   | ctt         | ata | caa | gcc   | atc | ttc | caa   | 738 |
| Asp | Ala | Glu   | Leu   | Pro   | Asp  | Ile | Ser   | His   | Leu         | Ile | Gln | Ala   | Ile | Phe | Gln   |     |
|     |     | 200   |       |       |      |     | 205   |       |             |     |     | 210   |     |     |       |     |
| gga | tat | ttt   | gca   | tat   | tca  | ggg | gag   | ctg   | aag         | aag | ccc | aga   | aca | aca | att   | 786 |
| Gly | Tyr | Phe   | Ala   | Tyr   | Ser  | Gly | Glu   | Leu   | Lys         | Lys | Pro | Arg   | Thr | Thr | Ile   |     |
|     | 215 |       |       |       |      | 220 |       |       |             |     | 225 |       |     |     |       |     |
| ccc | aaa | tgc   | ata   | ttt   | act  | gcg | tta   | cct   | ctg         | gtg | act | gta   | gtt | tat | tta   | 834 |
| Pro | Lys | Cys   | Ile   | Phe   | Thr  | Ala | Leu   | Pro   | Leu         | Val | Thr | Val   | Val | Tyr | Leu   |     |
| 230 |     |       |       |       | 235  |     |       |       |             | 240 |     |       |     |     | 245   |     |
| ctg | gtt | aac   | att   | tcc   | tat  | ctg | act   | gtt   | ctg         | aca | ccc | agg   | gaa | att | ctc   | 882 |
| Leu | Val | Asr   | ı Ile | Ser   | Tyr  | Leu | Thr   | Val   | Leu         | Thr | Pro | Arg   | Glu | Ile | e Leu |     |
|     |     |       |       | 250   | )    |     |       |       | 255         | •   |     |       |     | 260 | )     |     |
| tct | tea | a gat | t gct | gta   | gct  | ato | aca   | tgg   | gct<br>سندر | gat | cga | a gct | ttt | cce | c tca | 930 |
| Sa. | - 5 |       | . 41. | . Val | Δ1 a | 110 | . ፐኮታ | · Arr | -           | Acn | Are | , A1a | Pha | Pr  | Ser   |     |

|     |      |       | 265  |       |       |       |      | 270  |       |      |      |      | 275  |      |     |      |
|-----|------|-------|------|-------|-------|-------|------|------|-------|------|------|------|------|------|-----|------|
| tta | gca  | tgg   | att  | atg   | cct   | ttt   | gct  | att  | tct   | acc  | tca  | tta  | ttt  | agc  | aac | 978  |
| Leu | Ala  | Trp   | Ile  | Met   | Pro   | Phe   | Ala  | Ile  | Ser   | Thr  | Ser  | Leu  | Phe  | Ser  | Asn |      |
|     |      | 280   |      |       |       |       | 285  |      |       |      |      | 290  |      |      |     |      |
| ctt | ctg  | att   | tct  | ata   | ttt   | aaa   | tct  | tcg  | aga   | cca  | ata  | tat  | ctt  | gca  | agc | 1026 |
| Leu | Leu  | Ile   | Ser  | Ile   | Phe   | Lys   | Ser  | Ser  | Arg   | Pro  | Ile  | Tyr  | Leu  | Ala  | Ser |      |
|     | 295  |       |      |       |       | 300   |      |      |       |      | 305  |      |      |      |     |      |
| caa | gag  | ggc   | cag  | ctg   | cct   | ttg   | cta  | ttt  | aat   | aca  | ctt  | aat  | agt  | cac  | tct | 1074 |
| Gln | Glu  | Gly   | Gln  | Leu   | Pro   | Leu   | Leu  | Phe  | Asn   | Thr  | Leu  | Asn  | Ser  | His  | Ser |      |
| 310 |      |       |      |       | 315   |       |      |      |       | 320  |      |      |      |      | 325 |      |
| tct | cca  | ttt   | aca  | gct   | gtg   | cta   | cta  | ctt  | gtc   | act  | ttg  | gga  | tcc  | ctt  | gca | 1122 |
| Ser | Pro  | Phe   | Thr  | Ala   | Val   | Leu   | Leu  | Leu  | Val   | Thr  | Leu  | Gly  | Ser  | Leu  | Ala |      |
|     |      |       |      | 330   |       |       |      |      | 335   |      |      |      |      | 340  |     |      |
| att | atc  | tta   | aca  | agt   | cta   | att   | gat  | ttg  | ata   | aac  | tat  | att  | ttt  | ttc  | acg | 1170 |
| Ile | Ile  | Leu   | Thr  | Ser   | Leu   | Ile   | Asp  | Leu  | Ile   | Asn  | Tyr  | Ile  | Phe  | Phe  | Thr |      |
|     |      |       | 345  |       |       |       |      | 350  |       |      |      |      | 355  |      |     |      |
| ggt | tca  | tta   | tgg  | tct   | ata   | tta   | tta  | atg  | ata   | gga  | ata  | cta  | agg  | cgg  | aga | 1218 |
| Gly | Ser  | Leu   | Trp  | Ser   | Ile   | Leu   | Leu  | Met  | Ile   | Gly  | Ile  | Leu  | Arg  | Arg  | Arg |      |
|     |      | 360   |      |       | •     |       | 365  |      |       |      |      | 370  |      |      |     |      |
| tac | cag  | gaa   | ccc  | aat   | cta   | tct   | ata  | cct  | tat   | aag  | gta  | aaa  | ttg  | gat  | ttc | 1266 |
| Tyr | Gln  | Glu   | Pro  | Asn   | Leu   | Ser   | Ile  | Pro  | Tyr   | Lys  | Val  | Lys  | Leu  | Asp  | Phe |      |
|     | 375  |       |      |       |       | 380   |      |      |       |      | 385  |      |      |      |     |      |
| taa | t tc | tttt  | ctgt | gtg   | aaata | aac a | agat | attg | ag ta | ataa | ctgt | a tt | taag | atta |     | 1320 |
| taa | tcag | agc : | atct | ataa. | gt a  | gatc  | ttct | g aa | tact  | cagt | tac  | tgtg | aaa  | caca | tg  | 1376 |

| (210 | > 82 |      |       |      |     |     |     |      |             |     |     |     |     |     |     |     |
|------|------|------|-------|------|-----|-----|-----|------|-------------|-----|-----|-----|-----|-----|-----|-----|
| <211 | > 23 | 92   |       |      |     |     |     |      |             |     |     |     |     |     |     |     |
| <212 | > DN | A    |       |      |     |     |     |      |             |     |     |     |     |     |     |     |
| <213 | > Ho | mo s | apie  | ns   |     |     |     |      |             |     |     |     |     |     |     |     |
| <220 | >    |      |       |      |     |     |     |      |             |     |     |     |     |     |     |     |
| <221 | > CD | S    |       |      |     |     |     |      |             |     |     |     |     |     |     |     |
| <222 | > (2 | 2)   | . (10 | 68)  |     |     |     |      |             |     |     |     |     |     |     |     |
| <400 | > 82 |      |       |      |     |     |     |      |             |     |     |     |     |     |     |     |
| gaag | ggto | gt t | ggtg  | ggaa | a g | atg | gcg | gcg  | act         | ctg | gga | ссс | ctt | ggg | tcg | 51  |
|      |      |      |       |      |     | Met | Ala | Ala  | Thr         | Leu | Gly | Pro | Leu | Gly | Ser |     |
|      |      |      |       |      |     | 1   |     |      |             | 5   |     |     |     |     | 10  |     |
| tgg  | cag  | cag  | tgg   | cgg  | cga | tgt | ttg | tcg  | gct         | cgg | gat | ggg | tcc | agg | atg | 99  |
| Trp  | Gln  | Gln  | Trp   | Arg  | Arg | Cys | Leu | Ser  | Ala         | Arg | Asp | Gly | Ser | Arg | Met |     |
|      |      |      |       | 15   |     |     |     |      | 20          |     |     |     |     | 25  |     |     |
| tta  | ctc  | ctt  | ctt   | ctt  | ttg | ttg | ggg | tct  | ggg         | cag | ggg | cca | cag | caa | gtc | 147 |
| Leu  | Leu  | Leu  | Leu   | Leu  | Leu | Leu | Gly | Ser  | Gly         | G1n | G1y | Pro | Gln | Gln | Val |     |
|      |      |      | 30    |      |     |     |     | 35   |             |     |     |     | 40  |     |     |     |
| ggg  | gcg  | ggt  | caa   | acg  | ttc | gag | tac | ttg  | aaa         | cgg | gag | cac | tcg | ctg | tcg | 195 |
| Gly  | Ala  | Gly  | Gln   | Thr  | Phe | Glu | Tyr | Leu  | Lys         | Arg | Glu | His | Ser | Leu | Ser |     |
|      |      | 45   |       |      |     |     | 50  |      |             |     |     | 55  |     |     |     |     |
| aag  | ccc  | tac  | cag   | ggt  | gtg | ggc | aca | ggc  | agt         | tcc | tca | ctg | tgg | aat | ctg | 243 |
| Lys  | Pro  | Tyr  | Gln   | Gly  | Val | Gly | Thr | G1 y | Ser         | Ser | Ser | Leu | Trp | Asn | Leu |     |
|      | 60   |      |       |      |     | 65  |     |      |             |     | 70  |     |     |     |     |     |
| atg  | ggc  | aat  | gcc   | atg  | gtg | atg | acc | cag  | tat<br>نــر | atc | cgc | ctt | acc | cca | gat | 291 |

Met Gly Asn Ala Met Val Met Thr Gln Tyr Ile Arg Leu Thr Pro Asp

| <b>7</b> 5 |     |     |     |     | 80   |     |     |      |     | 85  |     |     |     |     | 90  |     |
|------------|-----|-----|-----|-----|------|-----|-----|------|-----|-----|-----|-----|-----|-----|-----|-----|
| atg        | caa | agt | aaa | cag | ggt  | gcc | ttg | tgg  | aac | cgg | gtg | cca | tgt | ttc | ctg | 339 |
| Met        | Gln | Ser | Lys | Gln | Gly  | Ala | Leu | Trp  | Asn | Arg | Val | Pro | Cys | Phe | Leu |     |
|            |     |     |     | 95  |      |     |     |      | 100 |     |     |     |     | 105 |     |     |
| aga        | gac | tgg | gag | ttg | cag  | gtg | cac | ttc  | aaa | atc | cat | gga | caa | gga | aag | 387 |
| Arg        | Asp | Trp | Glu | Leu | Gln  | Val | His | Phe  | Lys | Ile | His | Gly | Gln | G1y | Lys |     |
|            |     |     | 110 |     |      |     |     | 115  |     |     |     |     | 120 |     |     |     |
| aag        | aat | ctg | cat | ggg | gat  | ggc | ttg | gca  | atc | tgg | tac | aca | aag | gat | cgg | 435 |
| Lys        | Asn | Leu | His | Gly | Asp  | Gly | Leu | Ala  | Ile | Trp | Tyr | Thr | Lys | Asp | Arg |     |
|            |     | 125 |     |     |      |     | 130 |      |     |     |     | 135 |     |     |     |     |
| atg        | cag | cca | ggg | cct | gtg  | ttt | gga | aac  | atg | gac | aaa | ttt | gtg | ggg | ctg | 483 |
| Met        | Gln | Pro | Gly | Pro | Val  | Phe | Gly | Asn  | Met | Asp | Lys | Phe | Val | Gly | Leu |     |
|            | 140 |     |     |     |      | 145 |     |      |     |     | 150 |     |     |     |     |     |
| gga        | gta | ttt | gta | gac | acc  | tac | ccc | aat  | gag | gag | aag | cag | caa | gag | cgg | 531 |
| Gly        | Val | Phe | Val | Asp | Thr  | Tyr | Pro | Asn  | Glu | Glu | Lys | Gln | Gln | Glu | Arg |     |
| 155        |     |     |     |     | 160  |     |     |      |     | 165 |     |     |     |     | 170 |     |
| gta        | ttc | ccc | tac | atc | tca  | gcc | atg | gtg  | aac | aac | ggc | tcc | ctc | agc | tat | 579 |
| Val        | Phe | Pro | Tyr | Ile | Ser  | Ala | Met | Val  | Asn | Asn | Gly | Ser | Leu | Ser | Tyr |     |
|            |     |     |     | 175 |      |     |     |      | 180 |     |     |     |     | 185 |     |     |
| gat        | cat | gag | cgg | gat | ggg  | cgg | cct | aca  | gag | ctg | gga | ggc | tgc | aca | gcc | 627 |
| Asp        | His | Glu | Arg | Asp | G1 y | Arg | Pro | Thr  | Glu | Leu | Gly | Gly | Cys | Thr | Ala |     |
|            |     |     | 190 |     |      |     |     | 195  |     |     |     |     | 200 |     |     |     |
| att        | gtc | cgc | aat | ctt | cat  | tac | gac | acc  | ttc | ctg | gtg | att | cgc | tac | gtc | 675 |
| Ile        | Val | Arg | Asn | Leu | His  | Tyr | Asp | Thr, | Phe | Leu | Val | Ile | Arg | Tyr | Val |     |
|            |     | 205 |     |     |      |     | 210 |      |     |     |     | 215 |     |     |     |     |

| aag | agg | cat | ttg  | acg  | ata  | atg  | atg  | gat  | att        | gat  | ggc | aag  | cat  | gag | tgg | 723  |
|-----|-----|-----|------|------|------|------|------|------|------------|------|-----|------|------|-----|-----|------|
| Lys | Arg | His | Leu  | Thr  | Ile  | Met  | Met  | Asp  | Ile        | Asp  | Gly | Lys  | His  | Glu | Trp |      |
|     | 220 |     |      |      |      | 225  |      |      |            |      | 230 |      |      |     |     |      |
| agg | gac | tgc | att  | gaa  | gtg  | ccc  | gga  | gtc  | cgc        | ctg  | ccc | cgc  | ggc  | tac | tac | 771  |
| Arg | Asp | Cys | Ile  | Glu  | Val  | Pro  | Gly  | Val  | Arg        | Leu  | Pro | Arø  | Glv  | Tyr | Tyr |      |
| 235 |     |     |      |      | 240  |      |      |      |            | 245  |     |      |      |     | 250 |      |
| ttc | ggc | acc | tcc  | tcc  | atc  | act  | ggg  | gat  | ctc        | tca  | gat | aat  | cat  | gat | gtc | 819  |
| Phe | Gly | Thr | Ser  | Ser  | Ile  | Thr  | Gly  | Asp  | Leu        | Ser  | Asp | Asn  | His  | Asp | Val |      |
|     |     |     |      | 255  |      |      |      |      | 260        |      |     |      |      | 265 |     |      |
| att | tcc | ttg | aag  | ttg  | ttt  | gaa  | ctg  | aca  | gtg        | gag  | aga | acc  | cca  | gaa | gag | 867  |
| Ile | Ser | Leu | Lys  | Leu  | Phe  | Glu  | Leu  | Thr  | Val        | Glu  | Arg | Thr  | Pro  | Glu | Glu |      |
|     |     |     | 270  |      |      |      |      | 275  |            |      |     |      | 280  |     |     |      |
| gaa | aag | ctc | cat  | cga  | gat  | gtg  | ttc  | ttg  | ccc        | tca  | gtg | gac  | aat  | atg | aag | 915  |
| Glu | Lys | Leu | His  | Arg  | Asp  | Val  | Phe  | Leu  | Pro        | Ser  | Val | Asp  | Asn  | Met | Lys |      |
|     |     | 285 |      |      |      |      | 290  |      |            |      |     | 295  |      |     |     |      |
| ctg | cct | gag | atg  | aca  | gct  | cca  | ctg  | ccg  | ccc        | ctg  | agt | ggc  | ctg  | gcc | ctc | 963  |
| Leu | Pro | Glu | Met  | Thr  | Ala  | Pro  | Leu  | Pro  | Pro        | Leu  | Ser | Gly  | Leu  | Ala | Leu |      |
|     | 300 |     |      |      |      | 305  |      |      |            |      | 310 |      |      |     |     |      |
| ttc | ctc | atc | gtc  | ttt  | ttc  | tcc  | ctg  | gtg  | ttt        | tct  | gta | ttt  | gcc  | ata | gtc | 1011 |
| Phe | Leu | Ile | Val  | Phe  | Phe  | Ser  | Leu  | Val  | Phe        | Ser  | Val | Phe  | Ala  | Ile | Val |      |
| 315 |     |     |      |      | 320  |      |      |      |            | 325  |     |      |      |     | 330 |      |
| att | ggt | atc | ata  | ctc  | tac  | aac  | aaa  | tgg  | cag        | gaa  | cag | ago  | cga  | aag | cgc | 1059 |
| Ile | Gly | Ile | Ile  | Leu  | Tyr  | Asn  | Lys  | Trp  | Gln        | Glu  | Gln | Ser  | Arg  | Lys | Arg |      |
|     |     |     |      | 335  |      |      |      | ,    | 340<br>نىر |      |     |      |      | 345 |     |      |
| ttc | tac | toa | ge e | ctcc | tøct | g cc | acca | cťtt | tøt.       | gact | atc | acco | atoa | σσ  |     | 1110 |

Phe Tyr

| tatggaagga | gcaggcactg | gcctgagcat | gcagcctgga | gagtgttctt | gtctctagca | 1170 |
|------------|------------|------------|------------|------------|------------|------|
| gctggttggg | gactatattc | tgtcactgga | gttttgaatg | cagggacccc | gcattcccat | 1230 |
| ggttgtgcat | ggggacatct | aactctggtc | tgggaagcca | cccaccccag | ggcaatgctg | 1290 |
| ctgtgatgtg | cctttccctg | cagtccttcc | atgtgggagc | agaggtgtga | agagaattta | 1350 |
| cgtggttgtg | atgccaaaat | cacagaacag | aatttcatag | cccaggctgc | cgtgttgttt | 1410 |
| gactcagaag | gcccttctac | ttcagttttg | aatccacaaa | gaattaaaaa | ctggtaacac | 1470 |
| cacaggcttt | ctgaccatcc | attcgttggg | ttttgcattt | gacccaaccc | tctgcctacc | 1530 |
| tgaggagctt | tctttggaaa | ccaggatgga | aacttcttcc | ctgccttacc | ttcctttcac | 1590 |
| tccattcatt | gtcctctctg | tgtgcaacct | gagctgggaa | aggcatttgg | atgcctctct | 1650 |
| gttggggcct | ggggctgcag | aacacacctg | cgtttcactg | gccttcatta | ggtggcccta | 1710 |
| gggagatggc | tttctgcttt | ggatcactgt | tccctagcat | gggtcttggg | tctattggca | 1770 |
| tgtccatggc | cttcccaatc | aagtctcttc | aggccctcag | tgaagtttgg | ctaaaggttg | 1830 |
| gtgtaaaaat | caagagaagc | ctggaagaca | tcatggatgc | catggattag | ctgtgcaact | 1890 |
| gaccagetee | aggtttgatc | aaaccaaaag | caacatttgt | catgtggtct | gaccatgtgg | 1950 |
| agatgtttct | ggacttgcta | gagcctgctt | agctgcatgt | tttgtagtta | cgatttttgg | 2010 |
| aatcccactt | tgagtgctga | aagtgtaagg | aagctttctt | cttacacctt | gggcttggat | 2070 |
| attgcccaga | gaagaaattt | ggctttttt  | ttcttaatgg | acaagagaca | gttgctgttc | 2130 |
| tcatgttcca | agtctgagag | caacagaccc | tcatcatctg | tgcctggaag | agttcactgt | 2190 |
| cattgagcag | cacagcctga | gtgctggcct | ctgtcaaccc | ttattccact | gccttatttg | 2250 |
| acaaggggtt | acatgctgct | caccttactg | ccctgggatt | aaatcagtta | caggccagag | 2310 |
| tctccttgga | gggcctggaa | ctctgagtcc | tcctatgaac | ctctgtagcc | taaatgaaat | 2370 |
| tcttaaaatc | accgatggaa | ,cc        |            |            |            | 2392 |

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| <212            | > DN | IA    |       |      |      |      |       |     |       |      |      |      |       |     |     |     |
| <213            | > Hc | omo s | apie  | ns   |      |      |       |     |       |      |      |      |       |     |     |     |
| <220            | >    |       |       |      |      |      |       |     |       |      |      |      |       |     |     |     |
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| attg            | tccc | tg c  | ctgo  | ttct | g ga | gaaa | igaag | ata | ittga | icac | cato | tace | ggg ( | acc | atg | 57  |
|                 |      |       |       |      |      |      |       |     |       |      |      |      |       |     | Met |     |
|                 |      |       |       |      |      |      |       |     |       |      |      |      |       |     | 1   |     |
| gaa             | ctg  | ctt   | caa   | gtg  | acc  | att  | ctt   | ttt | ctt   | ctg  | ссс  | agt  | att   | tgc | agc | 105 |
| Glu             | Leu  | Leu   | Gln   | Val  | Thr  | Ile  | Leu   | Phẹ | Leu   | Leu  | Pro  | Ser  | Ile   | Cys | Ser |     |
|                 |      |       | 5     |      |      |      |       | 10  |       |      |      |      | 15    |     |     |     |
| agt             | aac  | agc   | aca   | ggt  | gtt  | tta  | gag   | gca | gct   | aat  | aat  | tca  | ctt   | gtt | gtt | 153 |
| Ser             | Asn  | Ser   | Thr   | Gly  | Val  | Leu  | Glu   | Ala | Ala   | Asn  | Asn  | Ser  | Leu   | Val | Val |     |
|                 |      | 20    |       |      |      |      | 25    |     |       |      |      | 30   |       |     |     |     |
| act             | aca  | aca   | aaa   | cca  | tct  | ata  | aca   | aca | cca   | aac  | aca  | gaa  | tca   | tta | cag | 201 |
| Thr             | Thr  | Thr   | Lys   | Pro  | Ser  | Ile  | Thr   | Thr | Pro   | Asn  | Thr  | Glu  | Ser   | Leu | Gln |     |
|                 | 35   |       |       |      |      | 40   |       |     |       |      | 45   |      |       |     |     |     |
| aaa             | aat  | gtt   | gtc   | aca  | cca  | aca  | act   | gga | aca   | act  | cct  | aaa  | gga   | aca | atc | 249 |
| Lys             | Asn  | Val   | Val   | Thr  | Pro  | Thr  | Thr   | Gly | Thr   | Thr  | Pro  | Lys  | Gly   | Thr | Ile |     |
| 50              |      |       |       |      | 55   |      |       |     |       | 60   |      |      |       |     | 65  |     |
| acc             | aat  | gaa   | tta   | ctt  | aaa  | atg  | tct   | ctg | atg   | tca  | aca  | gct  | act   | ttt | tta | 297 |
| Thr             | Asn  | Glu   | Leu   | Leu  | Lys  | Met  | Ser   | Leu | Met   | Ser  | Thr  | Ala  | Thr   | Phe | Leu |     |
|                 |      |       |       | 70   |      |      |       | /   | 75    |      |      |      |       | 80  |     |     |

| aca | agt | aaa | gat | gaa | gga | ttg | aaa | gcc | aca      | acc | act | gat | gtc | agg | aag | 345 |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|----------|-----|-----|-----|-----|-----|-----|-----|
| Thr | Ser | Lys | Asp | Glu | Gly | Leu | Lys | Ala | Thr      | Thr | Thr | Asp | Val | Arg | Lys |     |
|     |     | ·   | 85  |     |     |     |     | 90  |          |     | ٠   |     | 95  |     |     |     |
| aat | gac | tcc | atc | att | tca | aac | gta | aca | gta      | aca | agt | gtt | aca | ctt | cca | 393 |
| Asn | Asp | Ser | Ile | Ile | Ser | Asn | Val | Thr | Val      | Thr | Ser | Val | Thr | Leu | Pro |     |
|     |     | 100 |     |     |     |     | 105 |     |          |     |     | 110 |     |     |     |     |
| aat | gct | gtt | tca | aca | tta | caa | agt | tcc | aaa      | ссс | aag | act | gaa | act | cag | 441 |
| Asn | Ala | Val | Ser | Thr | Leu | G1n | Ser | Ser | Lys      | Pro | Lys | Thr | Glu | Thr | Gln |     |
|     | 115 |     |     |     |     | 120 |     |     |          |     | 125 |     |     |     |     |     |
| agt | tca | att | aaa | aca | aca | gaa | ata | cca | ggt      | agt | gtt | cta | caa | cca | gat | 489 |
| Ser | Ser | Ile | Lys | Thr | Thr | Glu | Ile | Pro | Gly      | Ser | Val | Leu | Gln | Pro | Asp |     |
| 130 |     |     |     |     | 135 |     |     |     |          | 140 |     |     |     |     | 145 |     |
| gca | tca | cct | tct | aaa | act | ggt | aca | tta | acc      | tca | ata | cca | gtt | aca | att | 537 |
| Ala | Ser | Pro | Ser | Lys | Thr | Gly | Thr | Leu | Thr      | Ser | Ile | Pro | Val | Thr | Ile |     |
|     |     |     |     | 150 |     |     |     |     | 155      |     |     |     |     | 160 |     |     |
| cca | gaa | aac | acc | tca | cag | tct | caa | gta | ata      | ggc | act | gag | ggt | gga | aaa | 585 |
| Pro | Glu | Asn | Thr | Ser | G1n | Ser | Gln | Val | Ile      | Gly | Thr | Glu | Gly | Gly | Lys |     |
|     |     |     | 165 |     |     |     |     | 170 |          |     |     |     | 175 |     |     |     |
| aat | gca | agc | act | tca | gca | acc | agc | cgg | tct      | tat | tcc | agt | att | att | ttg | 633 |
| Asn | Ala | Ser | Thr | Ser | Ala | Thr | Ser | Arg | Ser      | Tyr | Ser | Ser | Ile | Ile | Leu |     |
|     |     | 180 |     |     |     |     | 185 |     |          |     |     | 190 |     |     |     |     |
| ccg | gtg | gtt | att | gct | ttg | att | gta | ata | aca      | ctt | tca | gta | ttt | gtt | ctg | 681 |
| Pro | Val | Val | Ile | Ala | Leu | Ile | Val | Ile | Thr      | Leu | Ser | Val | Phe | Val | Leu |     |
|     | 195 |     |     |     |     | 200 |     |     | الداعلتي |     | 205 |     |     |     |     |     |
| gtg | ggt | ttg | tac | cga | atg | tgc | tgg | aag | gca      | gat | ccg | ggc | aca | cca | gaa | 729 |

| Val Gly Leu Tyr Arg Met Cys Trp Lys Ala Asp Pro Gly Thr Pro Glu   |                                      |
|---|--------------------------------------|
| 210 215 220 225   |                                      |
| aat gga aat gat caa cct cag tct gat aaa gag agc gtg aag ctt ctt   | 777                                  |
| Asn Gly Asn Asp Gln Pro Gln Ser Asp Lys Glu Ser Val Lys Leu Leu   |                                      |
| 230 235 240   |                                      |
| acc gtt aag aca att tet cat gag tet ggt gag cae tet gea caa gga   | 825                                  |
| Thr Val Lys Thr Ile Ser His Glu Ser Gly Glu His Ser Ala Gln Gly   |                                      |
| 245 250 255   |                                      |
| aaa acc aag aac tga cagcttgagg aattctctcc acacctaggc aataattacg   | 880                                  |
| Lys Thr Lys Asn   |                                      |
|   |                                      |
| 260   |                                      |
| 260 cttaatcttc agcttctatg caccaagcgt ggaaaaggag aaagtcctgc agaatcaatc   | 940                                  |
|   | 940<br>1000                          |
| cttaatcttc agcttctatg caccaagcgt ggaaaaggag aaagtcctgc agaatcaatc   |                                      |
| cttaatcttc agcttctatg caccaagcgt ggaaaaggag aaagtcctgc agaatcaatc ccgacttcca tacctgctgc tggactgtac cagacgtctg tcccagtaaa gtgatgtcca   | 1000                                 |
| cttaatcttc agcttctatg caccaagcgt ggaaaaggag aaagtcctgc agaatcaatc ccgacttcca tacctgctgc tggactgtac cagacgtctg tcccagtaaa gtgatgtcca gctgacatgc aataatttga tggaatcaaa aagaaceccg gggctctcct gttctctcac   | 1000<br>1060                         |
| cttaatcttc agcttctatg caccaagcgt ggaaaaggag aaagtcctgc agaatcaatc ccgacttcca tacctgctgc tggactgtac cagacgtctg tcccagtaaa gtgatgtcca gctgacatgc aataatttga tggaatcaaa aagaaceccg gggctctcct gttctctac atttaaaaat tccattactc catttacagg agcgttccta ggaaaaggaa ttttaggagg  | 1000<br>1060<br>1120                 |
| cttaatcttc agcttctatg caccaagcgt ggaaaaggag aaagtcctgc agaatcaatc ccgacttcca tacctgctgc tggactgtac cagacgtctg tcccagtaaa gtgatgtcca gctgacatgc aataatttga tggaatcaaa aagaaceccg gggctctcct gttctctcac atttaaaaat tccattactc catttacagg agcgttccta ggaaaaggaa ttttaggagg agaatttgtg agcagtgaat ctgacagccc aggaggtggg ctcgctgata ggcatgactt   | 1000<br>1060<br>1120<br>1180         |
| cttaatcttc agcttctatg caccaagcgt ggaaaaggag aaagtcctgc agaatcaatc ccgacttcca tacctgctgc tggactgtac cagacgtctg tcccagtaaa gtgatgtcca gctgacatgc aataatttga tggaatcaaa aagaaccccg gggctctcct gttctctacc atttaaaaat tccattactc catttacagg agcgttccta ggaaaaggaa ttttaggagg agaatttgtg agcagtgaat ctgacagccc aggaggtggg ctcgctgata ggcatgactt tccttaatgt ttaaagtttt ccgggccaag aatttttatc catgaagact ttcctacttt | 1000<br>1060<br>1120<br>1180<br>1240 |

⟨210⟩ 84

⟨211⟩ 1347

<212> DNA

<213> Homo sapiens

| <220 | >     |       |       |      |      |     |     |     |            |     |     |     |     |     |     |     |
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| <221 | > CI  | S.    |       |      |      |     |     |     |            |     |     |     |     |     |     |     |
| <222 | ?> (2 | 26)   | . (69 | 94)  |      |     |     |     |            |     |     |     |     | •   |     | •   |
| <400 | )> 84 | Į     |       |      |      |     |     |     |            |     |     |     |     |     |     |     |
| gcct | tgtg  | gtt t | tcca  | ccct | g aa | aga | atg | ttg | tgg        | ctg | ctc | ttt | ttt | ctg | gtg | 52  |
|      |       |       |       |      |      |     | Met | Leu | Trp        | Leu | Leu | Phe | Phe | Leu | Val |     |
|      |       |       |       |      |      |     | 1   |     |            |     | 5   |     |     |     |     |     |
| act  | gcc   | att   | cat   | gct  | gaa  | ctc | tgt | caa | cca        | ggt | gca | gaa | aat | gct | ttt | 100 |
| Thr  | Ala   | Ile   | His   | Ala  | Glu  | Leu | Cys | Gln | Pro        | Gly | Ala | Glu | Asn | Ala | Phe |     |
| 10   |       |       |       |      | 15   |     |     |     |            | 20  |     |     |     |     | 25  |     |
| aaa  | gtg   | aga   | ctt   | agt  | atc  | aga | aca | gct | ctg        | gga | gat | aaa | gca | tat | gcc | 148 |
| Lys  | Val   | Arg   | Leu   | Ser  | Ile  | Arg | Thr | Ala | Leu        | Gly | Asp | Lys | Ala | Tyr | Ala |     |
|      |       |       |       | 30   |      |     |     |     | <b>3</b> 5 |     |     |     |     | 40  |     |     |
| tgg  | gat   | acc   | aat   | gaa  | gaa  | tac | ctc | ttc | aaa        | gcg | atg | gta | gct | ttc | tcc | 196 |
| Trp  | Asp   | Thr   | Asn   | Glu  | Glu  | Tyr | Leu | Phe | Lys        | Ala | Met | Val | Ala | Phe | Ser |     |
|      |       |       | 45    |      |      |     |     | 50  |            |     |     |     | 55  |     |     |     |
| atg  | aga   | aaa   | gtt   | ccc  | aac  | aga | gaa | gca | aca        | gaa | att | tcc | cat | gtc | cta | 244 |
| Met  | Arg   | Lys   | Val   | Pro  | Asn  | Arg | Glu | Ala | Thr        | Glu | Ile | Ser | His | Val | Leu |     |
|      |       | 60    |       |      |      |     | 65  |     |            |     |     | 70  |     |     |     |     |
| ctt  | tgc   | aat   | gta   | acc  | cag  | agg | gta | tca | ttc        | tgg | ttt | gtg | gtt | aca | gac | 292 |
| Leu  | Cys   | Asn   | Val   | Thr  | Gln  | Arg | Val | Ser | Phe        | Trp | Phe | Val | Val | Thr | Asp |     |
|      | 75    |       |       |      |      | 80  |     |     |            |     | 85  |     |     |     |     |     |
| cct  | tca   | aaa   | aat   | cac  | acc  | ctt | cct | gct | gtt        | gag | gtg | caa | tca | gcc | ata | 340 |
| Pro  | Ser   | Lys   | Asn   | His  | Thr  | Leu | Pro | Ala | Val.       | Glu | Val | Gln | Ser | Ala | Ile |     |
| 90   |       |       |       |      | 95   |     |     |     |            | 100 |     |     |     |     | 105 |     |

790

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| aga | atg | aac | aag | aac | cgg | atc  | aac  | aat  | gcc   | ttc  | ttt  | cta  | aat | gac  | caa | 388 |
|-----|-----|-----|-----|-----|-----|------|------|------|-------|------|------|------|-----|------|-----|-----|
| Arg | Met | Asn | Lys | Asn | Arg | Ile  | Asn  | Asn  | Ala   | Phe  | Phe  | Leu  | Asn | Asp  | Gln |     |
|     |     |     |     | 110 |     |      |      |      | 115   |      |      | ٠    |     | 120  |     |     |
| act | ctg | gaa | ttt | tta | aaa | atc  | cct  | tcc  | aca   | ctt  | gca  | cca  | ccc | atg  | gac | 436 |
| Thr | Leu | Glu | Phe | Leu | Lys | Ile  | Pro  | Ser  | Thr   | Leu  | Ala  | Pro  | Pro | Met  | Asp |     |
|     |     |     | 125 |     |     |      |      | 130  |       |      |      |      | 135 |      |     |     |
| cca | tct | gtg | ccc | atc | tgg | att  | att  | ata  | ttt   | ggt  | gtg  | ata  | ttt | tgc  | atc | 484 |
| Pro | Ser | Val | Pro | Ile | Trp | Ile  | Ile  | Ile  | Phe   | Gly  | Val  | Ile  | Phe | Cys  | Ile |     |
|     |     | 140 |     |     |     |      | 145  |      |       |      |      | 150  |     |      |     |     |
| atc | ata | gtt | gca | att | gca | cta  | ctg  | att  | tta   | tca  | ggg  | atc  | tgg | caa  | cgt | 532 |
| Ile | Ile | Val | Ala | Ile | Ala | Leu  | Leu  | Ile  | Leu   | Ser  | Gly  | Ile  | Trp | Gln  | Arg |     |
|     | 155 |     |     |     |     | 160  |      |      |       |      | 165  |      |     |      |     |     |
| aga | aga | aag | aac | aaa | gaa | cca  | tct  | gaa  | gtg   | gat  | gac  | gct  | gaa | gat  | aag | 580 |
| Arg | Arg | Lys | Asn | Lys | Glu | Pro  | Ser  | Glu  | Val   | Asp  | Asp  | Ala  | Glu | Asp  | Lys |     |
| 170 |     |     |     |     | 175 |      |      |      |       | 180  |      |      |     |      | 185 |     |
| tgt | gaa | aac | atg | atc | aca | att  | gaa  | aat  | ggc   | atc  | ccc  | tct  | gat | ccc  | ctg | 628 |
| Cys | Glu | Asn | Met | Ile | Thr | Ile  | Glu  | Asn  | Gly   | Ile  | Pro  | Ser  | Asp | Pro  | Leu |     |
|     |     |     |     | 190 |     |      |      |      | 195   |      |      |      |     | 200  |     |     |
| gac | atg | aag | gga | ggg | cat | att  | aat  | gat  | gcc   | ttc  | atg  | aca  | gag | gat  | gag | 676 |
| Asp | Met | Lys | Gly | Gly | His | Ile  | Asn  | Asp  | Ala   | Phe  | Met  | Thr  | Glu | Asp  | Glu |     |
|     |     |     | 205 |     |     |      |      | 210  |       |      |      |      | 215 |      |     |     |
| agg | ctc | acc | cct | ctc | tga | aggg | ct g | ttgt | tctg  | c tt | cctc | aaga | aat | taaa | cat | 730 |
| Arg | Leu | Thr | Pro | Leu |     |      |      |      |       |      |      |      |     |      |     |     |
|     |     | 220 | l   |     |     |      |      |      | ، ندر |      |      |      |     |      |     |     |
|     |     |     |     |     |     |      |      |      |       |      |      |      |     |      |     |     |

ttgtttctgt gtgactgctg agcatcctga aataccaaga gcagatcata tattttgttt

| caccattctt | cttttgtaat | aaattttgaa | tgtgcttgaa | agtgaaaagc | aatcaattat | 850  |
|------------|------------|------------|------------|------------|------------|------|
| acccaccaac | accactgaaa | tcataagcta | ttcacgactc | aaaatațtct | aaaatatttt | 910  |
| tctgacagta | tagtgtataa | atgtggtcat | gtggtatttg | tagttattga | tttaagcatt | 970  |
| tttagaaata | agatcaggca | tatgtatata | ttttcacact | tcaaagacct | aaggaaaaat | 1030 |
| aaattttcca | gtggagaata | catataatat | ggtgtagaaa | tcattgaaaa | tggatccttt | 1090 |
| ttgacgatca | cttatatcac | tctgtatatg | actaagtaaa | caaaagtgag | aagtaattat | 1150 |
| tgtaaatgga | tggataaaaa | tggaattact | catatacagg | gtggaatttt | atcctgttat | 1210 |
| cacaccaaca | gttgattata | tattttctga | atatcagccc | ctaataggac | aattctattt | 1270 |
| gttgaccatt | tctacaattt | gtaaaagtcc | aatctgtgct | aacttaataa | agtaataatc | 1330 |
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⟨210⟩ 85

<211> 2284

<212> DNA

<213> Homo sapiens

<220>

<221> CDS

⟨222⟩ (75)... (626)

<400> 85

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Met Gly Val Arg Val His Val Val Ala Ala Ser Ala

1 5 10

ctg ctg tat ttc atc ctg ctt tct ggg acg aga tgt gag gaa aac tgt 158 Leu Leu Tyr Phe Ile Leu Leu Ser Gly Thr Arg Cys Glu Glu Asn Cys

|     |     | 15  |     |     |     |     | 20  |     |           |     |     | 25  |     |     |     |     |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----------|-----|-----|-----|-----|-----|-----|-----|
| ggt | aat | cct | gaa | cat | tgc | ctg | acc | aca | gac       | tgg | gta | cat | ctc | tgg | tat | 206 |
| Gly | Asn | Pro | Glu | His | Cys | Leu | Thr | Thr | Asp       | Trp | Val | His | Leu | Trp | Tyr |     |
|     | 30  |     |     |     |     | 35  |     |     |           |     | 40  |     |     |     |     |     |
| ata | tgg | ttg | cta | gtg | gta | att | ggc | gcg | ctg       | ctt | ctc | ctg | tgt | ggc | ctg | 254 |
| Ile | Trp | Leu | Leu | Val | Val | Ile | Gly | Ala | Leu       | Leu | Leu | Leu | Cys | Gly | Leu |     |
| 45  |     |     |     |     | 50  |     |     |     |           | 55  |     |     |     |     | 60  |     |
| acg | tcc | ctg | tgc | ttc | cgc | tgc | tgc | tgt | ctg       | agc | cgc | cag | caa | aat | ggg | 302 |
| Thr | Ser | Leu | Cys | Phe | Arg | Cys | Cys | Cys | Leu       | Ser | Arg | Gln | Gln | Asn | Gly |     |
|     |     |     |     | 65  |     |     |     |     | 70        |     |     |     |     | 75  |     |     |
| gaa | gat | ggg | ggc | cca | cca | ccc | tgt | gaa | gtg       | acc | gtc | att | gct | ttc | gat | 350 |
| Glu | Asp | Gly | Gly | Pro | Pro | Pro | Cys | Glu | Val       | Thr | Val | Ile | Ala | Phe | Asp |     |
|     |     |     | 80  |     |     |     |     | 85  |           |     |     |     | 90  |     |     |     |
| cac | gac | agc | act | ctc | cag | agc | act | atc | aca       | tct | ctg | cag | tcg | gtg | ttt | 398 |
| His | Asp | Ser | Thr | Leu | Gln | Ser | Thr | Ile | Thr       | Ser | Leu | Gln | Ser | Val | Phe |     |
|     |     | 95  |     |     |     |     | 100 |     |           |     |     | 105 |     |     |     |     |
| ggc | cct | gca | gct | cgg | agg | atc | ctg | gct | gtg       | gct | cac | tcc | cac | agc | tcc | 446 |
| Gly | Pro | Ala | Ala | Arg | Arg | Ile | Leu | Ala | Val       | Ala | His | Ser | His | Ser | Ser |     |
|     | 110 |     |     |     |     | 115 |     |     |           |     | 120 |     |     |     |     |     |
| ctg | ggc | cag | ctg | ccc | tcc | tct | ttg | gac | acc       | ctc | cca | ggg | tat | gaa | gaa | 494 |
| Leu | Gly | Gln | Leu | Pro | Ser | Ser | Leu | Asp | Thr       | Leu | Pro | Gly | Tyr | Glu | Glu |     |
| 125 |     |     |     |     | 130 |     |     |     |           | 135 |     |     |     |     | 140 |     |
| gct | ctt | cac | atg | agt | cgc | ttc | aca | gta | gcc       | atg | tgc | ggg | cag | aaa | gca | 542 |
| Ala | Leu | His | Met | Ser | Arg | Phe | Thr | Val | Ala<br>سر | Met | Cys | Gly | Gln | Lys | Ala |     |
|     |     |     |     | 145 | ;   |     |     | 1   | 150       |     |     |     |     | 155 | ;   |     |

| cct  | gat   | cta          | ccc   | cca   | gta           | cct   | gaa   | gaa       | aag   | cag  | ctg  | cct   | cca   | aca   | gag  | 590     |
|------|-------|--------------|-------|-------|---------------|-------|-------|-----------|-------|------|------|-------|-------|-------|------|---------|
| Pro  | Asp   | Leu          | Pro   | Pro   | Val           | Pro   | Glu   | Glu       | Lys   | Gln  | Leu  | Pro   | Pro   | Thr   | Glu  |         |
|      |       |              | 160   |       |               |       |       | 165       |       |      |      |       | 170   |       |      |         |
| aag  | gag   | tcg          | act   | cga   | ata           | gtt   | gac   | tct       | tgg   | aac  | tgat | gag   | agc   | tgtca | att  | 640     |
| Lys  | Glu   | Ser          | Thr   | Arg   | Ile           | Val   | Asp   | Ser       | Trp   | Asn  |      |       |       |       |      | ٠       |
|      |       | 175          |       |       |               |       | 180   |           |       |      |      |       |       |       |      |         |
| ttai | taaat | ag           | gagte | ggagt | g at          | tgtc  | cagag | tci       | tgtgį | ggaa | aate | gaac  | cac a | ataci | ttt  | ct 700  |
| aaco | ctca  | aga :        | agtti | ttaag | ga tg         | ggca  | tctaa | a cad     | cato  | att  | ctat | ggga  | aaa 1 | gatgg | gttc | tt 760  |
| acto | cttcg | gtt          | cacag | ggcct | tt ta         | atato | cttcc | ga        | tacag | gaat | gcto | taat  | ttg   | ggaa  | ctct | aa 820  |
| ttti | tgtat | cc :         | aatgg | gccaa | a at          | tctg  | caagt | aat       | tctc  | tagc | caca | ctga  | att a | actad | taa  | ac 880  |
| cagg | gaaag | gca          | tcaag | ggtat | tc ti         | tgaa  | ttcct | tta       | acta  | attg | agte | gcata | ata ( | gaati | tcct | gt 940  |
| acco | cacat | ga           | tact  | gcaag | gt tg         | gtgt  | ctctc | tci       | tgtca | agct | aato | cact  | gc (  | ggtta | act  | gg 1000 |
| aaaa | agaäa | aga (        | caaca | agtgi | tc ag         | gcaca | agcca | ı tc      | gacat | taa  | tgca | ictga | aat : | gcate | gcat | ct 1060 |
| ttc  | ctcct | iga :        | gacag | gcaat | to ga         | attt  | tacac | cga       | aatga | acaa | tgat | cato  | ett a | agaca | agca | ca 1120 |
| acat | tacco | cac          | tcgga | atato | et aa         | aaag  | ctagg | g gat     | tggca | attg | ctga | ıtate | ggg ( | caaag | gaga | ac 1180 |
| acag | gtata | igt :        | attta | aagtg | go ca         | aaata | atcag | g to      | tttc  | tttc | tctc | tggt  | cc    | tacco | ctc  | ag 1240 |
| cagt | tatga | aaa :        | aacto | ccata | ac ta         | gtgc  | agtca | a cas     | gttgg | gatt | aatt | ctto  | cag   | ttcc1 | ccg  | ca 1300 |
| ctgo | caaad | cac          | atata | atgtg | gc go         | caca  | tgcat | gta       | ataco | ctgc | acco | tgti  | ttt   | aacto | ctaa | ag 1360 |
| gaat | tagte | gtt          | gctti | tacti | tc <b>t</b> 1 | ttcc  | tgtti | t tg      | cctg  | gacc | actt | aaag  | gcc : | acaa  | cacc | tc 1420 |
| tata | agtga | aca          | cacgo | ctagi | tc to         | ctag  | tggtg | g gc      | cctca | actg | ccad | ctag  | gag   | gagco | catg | gt 1480 |
| ggaa | aaaca | aca          | ctct  | ctcci | tt tį         | gagc  | ctato | c tge     | caca  | tctc | toga | gtto  | ctt   | ggago | caaa | aa 1540 |
| ctaa | aatgo | ctg          | aacta | aagco | ct g          | gttg  | agate | g ct      | tece  | atgg | acca | atgc  | cgc : | agca  | cagt | gc 1600 |
| taa  | tcta  | tcc          | acaa  | aacat | ta co         | cacc  | tccca | a aa      | gtat  | tatt | attg | ggaa  | aat   | cgag  | gaag | tg 1660 |
| acg  | caca  | ttt          | aggg  | aaaa  | ac ta         | actc  | accti | t aga     | agaa  | gtca | ctga | aato  | cct   | tttt  | tttt | tt 1720 |
| ttti | gagai | t <b>g</b> g | agtt: | ttgci | to t          | tgta  | godos | /<br>a gg | ntøø  | at ø | caat | taan  | atσ   | atet  | 200  | to 1786 |

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#### 178/307

| actgtaacct | ccacctcccg  | gattcaagca | attcttctgc | ctcagcttcc | cgactagctg | 1840 |
|------------|-------------|------------|------------|------------|------------|------|
| ggattacagc | tgcctgccac  | cgtgcccagc | taatttttgt | atttttagtg | gagagggggt | 1900 |
| ttcaccatgt | tggccagtct  | ggtctagaac | tcctgacgtc | aggtgatccg | cccaccttgg | 1960 |
| cctcccaaag | tgctggaatt  | agaggcctga | cccctgctc  | ctggcctgaa | atctttaaag | 2020 |
| ccgtttttc  | cctaaaaaaac | gggaaataat | aacacctcag | aaggtttttg | tgaagatcaa | 2080 |
| agaagctaaa | tatatgtggc  | atgatttgta | aagtgttatg | catatgtatg | ttattcttcc | 2140 |
| tactgtcttc | taaccttccc  | ttgcctgcta | tgacttatct | gagagccatg | ttcccattta | 2200 |
| tctttttgcc | aactatgtta  | ctgttgtcac | acctgaaatg | gctttgtttt | tatcaataaa | 2260 |
| tacttgttga | ttgtggtaaa  | cagc       |            |            |            | 2284 |

⟨210⟩ 86

⟨211⟩ 1737

<212> DNA

<213> Homo sapiens

<220>

<221> CDS

⟨222⟩ (236)...(1024)

<400> 86

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286

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| Gly | Lys | Thr | Phe | Ser | Gln | Leu | Gly | Ser | Trp        | Arg | Glu | Asp | Glu | Asn | Lys |   |     |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|------------|-----|-----|-----|-----|-----|-----|---|-----|
|     |     |     | 5   |     |     |     |     | 10  |            |     |     |     | 15  | •   |     |   |     |
| tca | atc | ctg | tcc | tcc | aaa | cca | gcc | att | ggc        | agc | aag | gct | gtc | aac | tac | • | 334 |
| Ser | Ile | Leu | Ser | Ser | Lys | Pro | Ala | Ile | Gly        | Ser | Lys | Ala | Val | Asn | Tyr |   |     |
|     |     | 20  |     |     |     |     | 25  |     |            |     |     | 30  |     |     |     |   |     |
| tcc | agc | acc | ggt | agc | agc | aag | tct | ttt | tgt        | tcc | tgt | gtg | cct | tgt | gaa |   | 382 |
| Ser | Ser | Thr | Gly | Ser | Ser | Lys | Ser | Phe | Cys        | Ser | Cys | Val | Pro | Cys | Glu |   |     |
|     | 35  |     |     |     |     | 40  |     |     |            |     | 45  |     |     |     |     |   |     |
| gga | act | gct | gat | gcc | agc | ttc | gtg | act | tgt        | ccc | acc | tgc | cag | ggc | agt |   | 430 |
| Gly | Thr | Ala | Asp | Ala | Ser | Phe | Val | Thr | Cys        | Pro | Thr | Cys | G1n | Gly | Ser |   |     |
| 50  |     |     |     |     | 55  |     |     |     |            | 60  |     |     |     |     | 65  |   |     |
| ggc | aag | att | ccc | caa | gag | ctg | gag | aag | cag        | ttg | gtg | gct | ctc | att | ccc |   | 478 |
| Gly | Lys | Ile | Pro | Gln | Glu | Leu | Glu | Lys | Gln        | Leu | Val | Ala | Leu | Ile | Pro |   |     |
|     |     |     |     | 70  |     |     |     |     | <b>7</b> 5 |     |     |     |     | 80  |     |   |     |
| tat | ggg | gac | cag | agg | ctg | aag | ссс | aag | cac        | acg | aag | ctc | ttt | gtg | ttc |   | 526 |
| Tyr | Gly | Asp | Gln | Arg | Leu | Lys | Pro | Lys | His        | Thr | Lys | Leu | Phe | Val | Phe |   |     |
|     |     |     | 85  |     |     |     |     | 90  |            |     |     |     | 95  |     |     |   |     |
| ctg | gcc | gtg | ctc | atc | tgc | ctg | gtg | acc | tcc        | tcc | ttc | atc | gtc | ttt | ttc |   | 574 |
| Leu | Ala | Val | Leu | Ile | Cys | Leu | Val | Thr | Ser        | Ser | Phe | Ile | Val | Phe | Phe |   |     |
|     |     | 100 |     |     |     |     | 105 |     |            |     |     | 110 |     |     |     |   |     |
| ctg | ttt | ccc | cgg | tcc | gtc | att | gtg | cag | cct        | gca | ggc | ctc | aac | tcc | tcc |   | 622 |
| Leu | Phe | Pro | Arg | Ser | Val | Ile | Val | Gln | Pro        | Ala | Gly | Leu | Asn | Ser | Ser |   |     |
|     | 115 |     |     |     |     | 120 |     |     |            |     | 125 |     |     |     |     |   |     |
| aca | gtg | gcc | ttt | gat | gag | gct | gat | atc | ţac        | ctc | aac | ata | acg | aat | atc |   | 670 |
| Thr | Val | Ala | Phe | Asp | Glu | Ala | Asp | Île | Tyr        | Leu | Asn | Ile | Thr | Asn | Ile |   |     |

| 130 |     |      |     |     | 135 |      |      |      |      | 140  |      |      |     |      | 145 |      |
|-----|-----|------|-----|-----|-----|------|------|------|------|------|------|------|-----|------|-----|------|
| tta | aac | atc  | tcc | aat | ggc | aac  | tac  | tac  | ссс  | att  | atg  | gtg  | aca | cag  | ctg | 718  |
| Leu | Asn | Ile  | Ser | Asn | Gly | Asn  | Tyr  | Tyr  | Pro  | Ile  | Met  | Val  | Thr | Gln  | Leu |      |
|     |     |      |     | 150 |     |      |      |      | 155  |      |      |      |     | 160  |     |      |
| acc | ctc | gag  | gtt | ctg | cac | ctg  | tcc  | ctc  | gtg  | gtg  | ggg  | cag  | gtt | tcc  | aac | 766  |
| Thr | Leu | Glu  | Val | Leu | His | Leu  | Ser  | Leu  | Val  | Val  | Gly  | G1n  | Val | Ser  | Asn |      |
|     |     |      | 165 |     |     |      |      | 170  |      |      |      |      | 175 |      |     |      |
| aac | ctt | ctc  | cta | cac | att | ggc  | cct  | ttg  | gcc  | agt  | gaa  | cag  | atg | ttt  | tac | 814  |
| Asn | Leu | Leu  | Leu | His | Ile | Gly  | Pro  | Leu  | Ala  | Ser  | Glu  | Gln  | Met | Phe  | Tyr |      |
|     |     | 180  |     |     |     |      | 185  |      |      |      |      | 190  |     |      |     |      |
| gca | gta | gct  | acc | aag | ata | cgg  | gat  | gaa  | aac  | aca  | tac  | aaa  | atc | tgt  | acc | 862  |
| Ala | Val | Ala  | Thr | Lys | Ile | Arg  | Asp  | Glu  | Asn  | Thr  | Tyr  | Lys  | Ile | Cys  | Thr |      |
|     | 195 |      |     |     |     | 200  |      |      |      |      | 205  |      |     |      |     |      |
| tgg | ctg | gaa  | atc | aaa | gtc | cac  | cat  | gtg  | ctt  | ttg  | cac  | atc  | cag | ggc  | acc | 910  |
| Trp | Leu | Glu  | Ile | Lys | Val | His  | His  | Val  | Leu  | Leu  | His  | Ile  | Gln | Gly  | Thr |      |
| 210 |     |      |     |     | 215 |      |      |      |      | 220  |      |      |     |      | 225 |      |
| ctg | acc | tgt  | tca | tac | ctg | agc  | cat  | tca  | gag  | cag  | ctg  | gtc  | ttt | cag  | agc | 958  |
| Leu | Thr | Cys  | Ser | Tyr | Leu | Ser  | His  | Ser  | Glu  | Gln  | Leu  | Val  | Phe | Gln  | Ser |      |
|     |     |      |     | 230 |     |      |      |      | 235  |      |      |      |     | 240  |     |      |
| tat | gaa | 'tat | gtg | gac | tgc | cga  | gga  | aac  | gca  | tct  | gtg  | ccc  | cac | cag  | ctg | 1006 |
| Tyr | Glu | Tyr  | Val | Asp | Cys | Arg  | Gly  | Asn  | Ala  | Ser  | Val  | Pro  | His | Gln  | Leu |      |
|     |     |      | 245 |     |     |      |      | 250  |      |      |      |      | 255 |      |     |      |
| acc | cct | cac  | cca | cca | tga | cctg | tc t | gctg | tccc | t gt | actc | cagg | cac | ctgc | aac | 1060 |
| Thr | Pro | His  | Pro | Pro |     |      |      |      |      |      |      |      |     |      |     |      |

| cctggtctat | atctcccaca | actccctggt | gactaaggaa | ggactacaga | ggctttgcca | 1120 |
|------------|------------|------------|------------|------------|------------|------|
| aaggagaagc | cctgcctcat | cacaccctta | cctcccaccc | cctcagcaca | ggaagcttgc | 1180 |
| tttgaagtta | acttcataca | cacacactca | tatcctccag | tttcccccag | attctttcag | 1240 |
| gggctgccat | cagattctgc | ccttggttag | ttttttgttt | tttttttgg  | tagagacaga | 1300 |
| gtctcactgt | tggtccaggt | tggttttgaa | ctcctgggct | caagcgatcc | tcccttcttg | 1360 |
| gcctcccaaa | gcacttggat | tacagatgtg | agcctgtgcc | tggctggtct | ttcttgagga | 1420 |
| aaatctgacc | tggcattttc | ttgaggcacc | ttagattccc | tggagtggca | cctggccttt | 1480 |
| ctgtactgag | cacctggtca | gtctgaaggg | ggcatttcac | cccagctcca | tcagggctgg | 1540 |
| cagtcccgtc | tgaatgtgga | gagagctgta | gttttatctg | gcttttaaaa | catggacctg | 1600 |
| ccggctgggc | gcagtggctt | acacctgtaa | tcccagtact | ttgggaggcc | gaagtgggtg | 1660 |
| gatcacttga | gggcaggagt | tcgtgaccag | cctggtcaac | atggtgaaac | cttgtctcta | 1720 |
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⟨222⟩ (103)... (609)

⟨400⟩ 87

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Met Gly Val Pro

| acg | gcc | ctg | gag | gcc | ggc | agc        | tgg | cgc | tgg       | gga | tcc | ctg | ctc | ttc | gct | 162 |
|-----|-----|-----|-----|-----|-----|------------|-----|-----|-----------|-----|-----|-----|-----|-----|-----|-----|
| Thr | Ala | Leu | Glu | Ala | Gly | Ser        | Trp | Arg | Trp       | Gly | Ser | Leu | Leu | Phe | Ala |     |
| 5   |     |     |     |     | 10  |            | •   |     |           | 15  |     |     |     |     | 20  |     |
| ctc | ttc | ctg | gct | gcg | tcc | cta        | ggc | aaa | gat       | gca | cca | tcc | aac | tgt | gtg | 210 |
| Leu | Phe | Leu | Ala | Ala | Ser | Leu        | Gly | Lys | Asp       | Ala | Pro | Ser | Asn | Cys | Val |     |
|     |     |     |     | 25  |     |            |     |     | 30        |     |     |     |     | 35  |     |     |
| gtg | tac | cca | tcc | tcc | tcc | cag        | gag | agt | gaa       | aac | atc | acg | gct | gca | gcc | 258 |
| Val | Tyr | Pro | Ser | Ser | Ser | Gln        | Glu | Ser | Glu       | Asn | Ile | Thr | Ala | Ala | Ala |     |
|     |     |     | 40  |     |     |            |     | 45  |           |     |     |     | 50  |     |     |     |
| ctg | gct | acg | ggt | gcc | tgc | atc        | gta | gga | atc       | ctc | tgc | ctc | ccc | ctc | atc | 306 |
| Leu | Ala | Thr | Gly | Ala | Cys | Ile        | Val | Gly | Ile       | Leu | Cys | Leu | Pro | Leu | Ile |     |
|     |     | 55  |     |     |     |            | 60  |     |           |     |     | 65  |     |     |     |     |
| ctg | ctc | ctg | gtc | tac | aag | caa        | agg | cag | gca       | gcc | tcc | aac | cgc | cgt | gcc | 354 |
| Leu | Leu | Leu | Val | Tyr | Lys | Gln        | Arg | Gln | Ala       | Ala | Ser | Asn | Arg | Arg | Ala |     |
|     | 70  |     |     |     |     | <b>7</b> 5 |     |     |           |     | 80  |     |     |     |     |     |
| cag | gag | ctg | gtg | cgg | atg | gac        | agc | aac | att       | caa | ggg | att | gaa | aac | ccc | 402 |
| Gln | Glu | Leu | Val | Arg | Met | Asp        | Ser | Asn | Ile       | Gln | Gly | Ile | Glu | Asn | Pro |     |
| 85  |     |     |     |     | 90  |            |     |     |           | 95  |     |     |     |     | 100 |     |
| ggc | ttt | gaa | gcc | tca | cca | cct        | gcc | cag | ggg       | ata | ccc | gag | gcc | aaa | gtc | 450 |
| Gly | Phe | Glu | Ala | Ser | Pro | Pro        | Ala | Gln | Gly       | Ile | Pro | Glu | Ala | Lys | Val |     |
|     |     |     |     | 105 |     |            |     |     | 110       |     |     |     |     | 115 | i   |     |
| agg | cac | ccc | ctg | tcc | tat | gtg        | gcc | cag | cgg       | cag | cct | tct | gag | tct | ggg | 498 |
| Arg | His | Pro | Leu | Ser | Tyr | Val        | Ala | Gln | Arg       | Gln | Pro | Ser | Glu | Ser | Gly |     |
|     |     |     | 120 | )   |     |            |     | 125 | ا<br>منسو |     |     |     | 130 | )   |     |     |
| cgg | cat | cts | ctt | tce | gag | ccc        | ago | acc | ccc       | ctg | tct | cct | cca | gge | ccc | 546 |

| Arg His Leu Leu Ser Glu Pro Ser Thr Pro Leu Ser Pro Pro Gly Pro    |      |
|--|------|
| 135 140 145  |      |
| gga gac gtc ttc ttc cca tcc ctg gac cct gtc cct gac tct cca aac    | 594  |
| Gly Asp Val Phe Phe Pro Ser Leu Asp Pro Val Pro Asp Ser Pro Asn    |      |
| 150 155 160  |      |
| ttt gag gtc atc tagc ccagctgggg gacagtgggc tgttgtggct gggtctgggg   | 650  |
| Phe Glu Val Ile  |      |
| 165  |      |
| caggtgcatt tgagccaggg ctggctctgt gagtggcctc cttggcctcg gccctggttc  | 710  |
| cetecetect getetggget cagatactgt gacateceag aageceagee ceteaacee   | 770  |
| tctggatgct acatggggat gctggacggc tcagcccctg ttccaaggat tttggggtgc  | 830  |
| tgagattctc ccctagagac ctgaaattca ccagctacag atgccaaatg acttacatct  | 890  |
| taagaagtct cagaacgtcc agcccttcag cagctctcgt tctgagacat gagccttggg  | 950  |
| atgtggcagc atcagtggga caagatggac actgggccac cctcccaggc accagacaca  | 1010 |
| gggcacggtg gagagacttc tcccccgtgg ccgccttggc tcccccgttt tgcccgaggc  | 1070 |
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| cactggccat cgccaccttc cccagctgcc tcctaccagc agtttctctg aagatctgtc  | 1190 |
| aacaggttaa gtcaatctgg ggcttccact gcctgcattc cagtccccag agcttggtgg  | 1250 |
| tcccgaaacg ggaagtacat attggggcat ggtggcctcc gtgagcaaat ggtgtcttgg  | 1310 |
| gcaatctgag gccaggacag atgttgcccc acccactgga gatggtgctg agggaggtgg  | 1370 |
| gtggggcctt ctgggaaggt gagtggagag gggcacctgc ccccgccct ccccatcccc   | 1430 |
| tactcccact gctcagcgcg ggccattgca agggtgccac acaatgtctt gtccaccctg  | 1490 |
| ggacacttct gagtatgaag cgggatgcta ttaaaaaacta catggggaaa caggtgcaaa | 1550 |
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| gggtctgttc ctagttgcaa cagttcttgg aaacccactc gagagggcca cgcctccatt | 180 |
| caccaggeca egeateacaa gaggeaacae caggagecaa e atg age teg ggg     | 233 |
| Met Ser Ser Gly   |     |
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| act gaa ctg ctg tgg ccc gga gca gcg ctg ctg gtg ctg ttg ggg gtg   | 281 |
| Thr Glu Leu Leu Trp Pro Gly Ala Ala Leu Leu Val Leu Leu Gly Val   |     |
| 5 10 15 20  |     |
| gca gcc agt ctg tgt gtg cgc tgc tca cgc cca ggt gca aag agg tca   | 329 |
| Ala Ala Ser Leu Cys Val Arg Cys Ser Arg Pro Gly Ala Lys Arg Ser   |     |
| 25 30 35  |     |
| gag aaa atc tac cag cag aga agt ctg cgt gag gac caa cag agc ttt   | 377 |
| Glu Lys Ile Tyr Gln Gln Arg Ser Leu Arg Glu Asp Gln Gln Ser Phe   |     |
| 40 45 50  |     |
| acg ggg tcc cgg acc tac tcc ttg gtc ggg cag gca tgg cca gga ccc   | 425 |
| Thr Gly Ser Arg Thr Tyr Ser Leu Vál Gly Gln Ala Trp Pro Gly Pro   |     |

|     |     | 55  |     |     |     |     | 60  |     |     |     |     | 65  |     |     |     |     |
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| ctg | gcg | gac | atg | gca | ccc | aca | agg | aag | gac | aag | ctg | ttg | caa | ttc | tac | 473 |
| Leu | Ala | Asp | Met | Ala | Pro | Thr | Arg | Lys | Asp | Lys | Leu | Leu | Gln | Phe | Tyr |     |
|     | 70  |     |     |     |     | 75  |     |     |     |     | 80  |     |     |     |     |     |
| ccc | agc | ctg | gag | gat | cca | gca | tct | tcc | agg | tac | cag | aac | ttc | agc | aaa | 521 |
| Pro | Ser | Leu | Glu | Asp | Pro | Ala | Ser | Ser | Arg | Tyr | Gln | Asn | Phe | Ser | Lys |     |
| 85  |     |     |     |     | 90  |     |     |     |     | 95  |     |     |     |     | 100 |     |
| gga | agc | aga | cac | ggg | tcg | gag | gaa | gcc | tac | ata | gac | ccc | att | gcc | atg | 569 |
| Gly | Ser | Arg | His | Gly | Ser | Glu | Glu | Ala | Tyr | Ile | Asp | Pro | Ile | Ala | Met |     |
|     |     |     |     | 105 |     |     |     |     | 110 |     |     |     |     | 115 |     |     |
| gag | tat | tac | aac | tgg | ggg | cgg | ttc | tcg | aag | ccc | cca | gaa | gat | gat | gat | 617 |
| Glu | Tyr | Tyr | Asn | Trp | Gly | Arg | Phe | Ser | Lys | Pro | Pro | Glu | Asp | Asp | Asp |     |
|     |     |     | 120 |     |     |     |     | 125 |     |     |     |     | 130 |     |     |     |
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| Ala | Asn | Ser | Tyr | Glu | Asn | Val | Leu | Ile | Cys | Lys | Gln | Lys | Thr | Thr | Glu |     |
|     |     | 135 |     |     |     |     | 140 |     |     | •   |     | 145 |     |     |     |     |
| aca | ggt | gcc | cag | cag | gag | ggc | ata | ggt | ggc | ctc | tgc | aga | ggg | gac | ctc | 713 |
| Thr | Gly | Ala | Gln | Gln | Glu | Gly | Ile | Gly | Gly | Leu | Cys | Arg | Gly | Asp | Leu |     |
|     | 150 |     |     |     |     | 155 |     |     |     |     | 160 |     |     |     |     |     |
| agc | ctg | tca | ctg | gcc | ctg | aag | act | ggc | ccc | act | tct | ggt | ctc | tgt | ccc | 761 |
| Ser | Leu | Ser | Leu | Ala | Leu | Lys | Thr | Gly | Pro | Thr | Ser | Gly | Leu | Cys | Pro |     |
| 165 |     |     |     |     | 170 |     |     |     |     | 175 |     |     |     |     | 180 |     |
| tct | gcc | tcc | ccg | gaa | gaa | gat | gag | gaa | tct | gag | gat | tat | cag | aac | tca | 809 |
| Ser | Ala | Ser | Pro | Glu | Glu | Asp | Glu | Glu | Şer | Glu | Asp | Tyr | Gln | Asn | Ser |     |
|     |     |     |     | 185 | I   |     |     |     | 190 |     |     |     |     | 195 | ,   |     |

| gca tcc atc cat cag tgg cgc gag tcc agg aag gtc atg ggg caa ctc  | 857      |
|--|----------|
| Ala Ser Ile His Gln Trp Arg Glu Ser Arg Lys Val Met Gly Gln Leu  |          |
| 200 205 210  |          |
| cag aga gaa gca tcc cct ggc ccg gtg gga agc cca gac gag gag gac  | 905      |
| Gln Arg Glu Ala Ser Pro Gly Pro Val Gly Ser Pro Asp Glu Glu Asp  |          |
| 215 220 225  |          |
| ggg gaa ccg gat tac gtg aat ggg gag gtg gca gcc aca gaa gcc      | 950      |
| Gly Glu Pro Asp Tyr Val Asn Gly Glu Val Ala Ala Thr Glu Ala      |          |
| 230 235 240  |          |
| tagggcagac caagaagaaa ggagccaagg caaagaggga ccactgtgct catggacco | a 1010   |
| tcgctgcctt ccaaggacca tttcccagag ctactcaact tttaagcccc tgccatggt | t 1070   |
| gctcctggaa ggagaaccag ccaccctgag gaccacctgg ccatgcgtgc acagcctgg | g 1130 . |
| aaaagacagt tactcacggg agctgcaggc ccgtcaccaa gccctctccc gacccaggc | t 1190   |
| ttgtggggca ggcacctggt accaagggta acccggctcc tggtatggac ggatgcgca | ig 1250  |
| gatttaggat aagetgteac ceagteecea taacaaaace aetgteeaac aetggtate | t 1310   |
| gtgttctttt gtgctatgaa tttggattcc taattgctat tgttggttgc tggggtttt | a 1370   |
| aatgattgat aagcttgtac agttaactta tagaggggga gccatattta acattctgg | ga 1430  |
| tttcagagta gagatttctg tgttgtctcc tagaaagcat tacatgtagt ttatttcag | gc 1490  |
| atccttgttg ggtggggccc tggctctctt cccctttggt gggacctccc ctttctttg | gg 1550  |
| gcttcagttc actcaggaag aaatgaggct gtcgccatct ttatgtgctt ccagtggaa | aa 1610  |
| tgtcacttgc tacagacaat agtgcatgag agtctagaga agtagtgacc agaacaggg | gc 1670  |
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| agttg  | 1855     |

| <210 | > 89  | •          |       |       |       |       |      |         |           |       |       |       |       |       |     |     |
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| <212 | ?> D! | <b>I</b> A |       |       |       |       |      |         |           |       |       |       |       |       |     |     |
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|      |       |            |       |       |       |       | Ме   | et Al   | la Ai     | ng Se | er Le | eu Cy | rs Pi | ro G  | ly  |     |
|      |       | -          |       |       |       |       |      | 1       |           |       |       | 5     |       |       |     | •   |
| gcc  | tgg   | cta        | agg   | aaa   | ccc   | tat   | tac  | ctc     | cag       | gct   | cgc   | ttc   | tca   | tat   | gtg | 99  |
| Ala  | Trp   | Leu        | Arg   | Lys   | Pro   | Tyr   | Tyr  | Leu     | Gln       | Ala   | Arg   | Phe   | Ser   | Tyr   | Val |     |
|      | 10    |            |       |       |       | 15    |      |         |           |       | 20    |       |       |       |     |     |
| cgg  | atg   | aaa        | tat   | ctt   | ttc   | ttt   | tcc  | tgg     | tta       | gtg   | gtt   | ttt   | gtt   | gga   | agc | 147 |
| Arg  | Met   | Lys        | Tyr   | Leu   | Phe   | Phe   | Ser  | Trp     | Leu       | Val   | Va1   | Phe   | Val   | Gly   | Ser |     |
| 25   |       |            |       |       | 30    |       |      |         |           | 35    |       |       |       |       | 40  |     |
| tgg  | att   | ata        | tat   | gtg   | cag   | tat   | tct  | acc     | tat       | aca   | gaa   | tta   | tgc   | aga   | gga | 195 |
| Trp  | Ile   | Ile        | Tyr   | Val   | Gln   | Tyr   | Ser  | Thr     | Tyr       | Thr   | Glu   | Leu   | Cys   | Arg   | Gly |     |
|      |       |            |       | 45    |       |       |      |         | 50        |       |       |       |       | 55    |     |     |
| aag  | gac   | tgt        | aag   | aaa   | ata   | ata   | tgt  | gac     | aag       | tac   | aag   | act   | gga   | gtt   | att | 243 |
| Lys  | Asp   | Cys        | Lys   | Lys   | Ile   | Ile   | Cys  | Asp     | Lys       | Tyr   | Lys   | Thr   | Gly   | Val   | Ile |     |
|      |       |            | 60    |       |       |       |      | 65<br>⁄ | ۰۰۰ کنتمو |       |       |       | 70    |       |     |     |
| gat  | ggg   | cct        | gca   | tgt   | aac   | agc   | ctt  | tgt     | gtt       | aca   | gaa   | act   | ctt   | tac   | ttt | 291 |

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| Asp | Gly | Pro   | Ala | Cys   | Asn | Ser   | Leu | Cys   | Val        | Thr   | Glu | Thr | Leu   | Tyr   | Phe   |     |
|-----|-----|-------|-----|-------|-----|-------|-----|-------|------------|-------|-----|-----|-------|-------|-------|-----|
|     |     | 75    |     |       |     |       | 80  |       |            |       |     | 85  |       |       |       |     |
| gga | aaa | tgt   | tta | tcc   | acc | aag   | ссс | aac   | aat        | cag   | atg | tat | tta   | ggg   | att   | 339 |
| Gly | Lys | Cys   | Leu | Ser   | Thr | Lys   | Pro | Asn   | Asn        | Gln   | Met | Tyr | Leu   | Gly   | Ile   |     |
|     | 90  |       |     |       |     | 95    |     |       |            |       | 100 |     |       |       |       |     |
| tgg | gat | aat   | cta | cca   | ggt | gtt   | gtg | aaa   | tgt        | caa   | atg | gaa | caa   | gcg   | ctt   | 387 |
| Trp | Asp | Asn   | Leu | Pro   | Gly | Val   | Val | Lys   | Cys        | Gln   | Met | Glu | Gln   | Ala   | Leu   |     |
| 105 |     |       |     |       | 110 |       |     |       |            | 115   |     |     |       |       | 120   |     |
| cat | ctt | gat   | ttt | gga   | act | gaa   | ttg | gaa   | cca        | aga   | aaa | gaa | ata   | gtg   | cta   | 435 |
| His | Leu | Asp   | Phe | Gly   | Thr | Glu   | Leu | Glu   | Pro        | Arg   | Lys | Glu | Ile   | Val   | Leu   |     |
|     |     |       |     | 125   |     |       |     |       | 130        |       |     |     |       | 135   |       |     |
| ttt | gat | aag   | cca | act   | aga | gga   | act | act   | gta        | caa   | aaa | ttt | aaa   | gaa   | atg   | 483 |
| Phe | Asp | Lys   | Pro | Thr   | Arg | Gly   | Thr | Thr   | Val        | Gln   | Lys | Phe | Lys   | Glu   | Met   |     |
|     |     |       | 140 |       |     |       |     | 145   |            |       |     |     | 150   |       |       |     |
| gtc | tat | agt   | ctc | ttt   | aag | gca   | aaa | ttg   | ggt        | gac   | caa | ġga | aac   | ctc   | tct   | 531 |
| Val | Tyr | Ser   | Leu | Phe   | Lys | Ala   | Lys | Leu   | Gly        | Asp   | Gln | Gly | Asn   | Leu   | Ser   |     |
|     |     | 155   |     |       |     |       | 160 |       |            |       |     | 165 |       |       |       |     |
| gaa | ctg | gtt   | aat | ctc   | atc | ttg   | acg | gtg   | gct        | gat   | gga | gac | aaa   | gat   | ggc   | 579 |
| Glu | Leu | Val   | Asn | Leu   | Ile | Leu   | Thr | Val   | Ala        | Asp   | Gly | Asp | Lys   | Asp   | Gly   | ٠   |
|     | 170 |       |     |       |     | 175   |     |       |            |       | 180 |     |       |       |       |     |
| cag | gtt | tcc   | ttg | gga   | gaa | gca   | aag | tcg   | gca        | tgg   | gca | ctt | ctt   | caa   | ctg   | 627 |
| Gln | Val | Ser   | Leu | Gly   | Glu | Ala   | Lys | Ser   | Ala        | Trp   | Ala | Leu | Leu   | Glr   | ı Leu |     |
| 185 | i   |       |     |       | 190 | )     |     |       |            | 195   |     |     |       |       | 200   |     |
| aat | gaa | ttt   | ctt | ctc   | atg | gtg   | ata | ctt   | caa<br>سنر | gat   | aaa | gaa | cat   | aco   | ccc   | 675 |
| Asn | Glu | ı Phe | Leu | ı Leu | Met | . Val | Ile | . Léu | Glr        | ı Asp | Lys | Glu | ı His | s Thi | r Pro |     |

|     |     |     |     | 205 |                  |     |     |     | 210          |      |     |     |     | 215 |     |      |
|-----|-----|-----|-----|-----|------------------|-----|-----|-----|--------------|------|-----|-----|-----|-----|-----|------|
| aaa | tta | atg | gga | ttc | tgt              | ggt | gac | ctc | tat          | gtg. | atg | gaa | agt | gtt | gaa | 723  |
| Lys | Leu | Met | Gly | Phe | Cys              | Gly | Asp | Leu | Tyr          | Val  | Met | Glu | Ser | Val | Glu |      |
|     |     |     | 220 |     |                  |     |     | 225 |              |      |     |     | 230 |     |     |      |
| tat | acc | tct | ctt | tat | gga              | ata | agc | ctt | cct          | tgg  | gtc | att | gaa | ctt | ttt | 771  |
| Tyr | Thr | Ser | Leu | Tyr | Gly              | Ile | Ser | Leu | Pro          | Trp  | Val | Ile | Glu | Leu | Phe |      |
|     |     | 235 |     |     |                  |     | 240 |     |              |      |     | 245 |     |     |     |      |
| att | cca | tct | ggg | ttc | aga              | aga | agc | atg | gat          | cag  | ctg | ttc | aca | cca | tca | 819  |
| Ile | Pro | Ser | Gly | Phe | Arg              | Arg | Ser | Met | Asp          | Gln  | Leu | Phe | Thr | Pro | Ser |      |
|     | 250 |     |     |     |                  | 255 |     |     |              |      | 260 |     |     |     |     |      |
| tgg | cca | aga | aag | gcc | aaa <sup>·</sup> | ata | gcc | ata | gga          | ctt  | cta | gaa | ttt | gtg | gaa | 867  |
| Trp | Pro | Arg | Lys | Ala | Lys              | Ile | Ala | Ile | Gly          | Leu  | Leu | Glu | Phe | Val | Glu |      |
| 265 |     |     |     |     | 270              |     |     |     |              | 275  |     |     |     |     | 280 |      |
| gat | gtt | ttc | cat | ggc | ссс              | tac | gga | aat | ttc          | ctc  | atg | tgc | gat | act | agt | 915  |
| Asp | Val | Phe | His | Gly | Pro              | Tyr | Gly | Asn | Phe          | Leu  | Met | Cys | Asp | Thr | Ser |      |
|     |     |     |     | 285 |                  |     |     |     | 290          |      |     |     |     | 295 |     |      |
| gcc | aaa | aac | cta | gga | tat              | aat | gat | aag | tat          | gat  | ttg | aaa | atg | gtg | gat | 963  |
| Ala | Lys | Asn | Leu | Gly | Tyr              | Asn | Asp | Lys | Tyr          | Asp  | Leu | Lys | Met | Val | Asp |      |
|     |     |     | 300 |     |                  |     |     | 305 |              |      |     |     | 310 |     |     |      |
| atg | aga | aaa | att | gtg | cca              | gag | aca | aac | ctg          | aaa  | gaa | ctt | att | aag | gat | 1011 |
| Met | Arg | Lys | Ile | Val | Pro              | Glu | Thr | Asn | Leu          | Lys  | Glu | Leu | Ile | Lys | Asp |      |
|     |     | 315 |     |     |                  |     | 320 |     |              |      |     | 325 |     |     |     |      |
| cgt | cac | tgt | gag | tct | gat              | ttg | gac | tgt | gtc          | tat  | ggc | aca | gat | tgt | aga | 1059 |
| Arg | His | Cys | Glu | Ser | Asp              | Leu | Asp | Cys | Y <u>a</u> l | Tyr  | Gly | Thr | Asp | Cys | Arg |      |
|     | 330 |     |     |     |                  | 335 |     | /   |              |      | 340 |     |     |     |     | W    |

| act agc tgt gat cag agt aca atg aag tgt act tca gaa gtg ata caa    | 1107 |
|--|------|
| Thr Ser Cys Asp Gln Ser Thr Met Lys Cys Thr Ser Glu Val Ile Gln    |      |
| 345 350 355 360  |      |
| cca aac ttg gca aaa gct tgt cag tta ctc aaa gac tac cta ctg cgt    | 1155 |
| Pro Asn Leu Ala Lys Ala Cys Gln Leu Leu Lys Asp Tyr Leu Leu Arg    |      |
| 365 370 375  |      |
| ggt gct cca agt gaa att cgt gaa gaa tta gaa aag cag ctt tat tct    | 1203 |
| Gly Ala Pro Ser Glu Ile Arg Glu Glu Leu Glu Lys Gln Leu Tyr Ser    |      |
| 380 385 390  |      |
| tgt att gct ctc aaa gtc aca gca aat caa atg gaa atg gaa cat tct    | 1251 |
| Cys Ile Ala Leu Lys Val Thr Ala Asn Gln Met Glu Met Glu His Ser    |      |
| 395 400 405  |      |
| ttg ata cta aat aac cta aaa aca tta ttg tgg aag aaa att tcc tac    | 1299 |
| Leu Ile Leu Asn Asn Leu Lys Thr Leu Leu Trp Lys Lys Ile Ser Tyr    |      |
| 410 415 420  |      |
| act aat gac tot tagttoatt tggacataat taccatttta agaaacctgo         | 1350 |
| Thr Asn Asp Ser  |      |
| 425  |      |
| cacttttaaa gaacaatttt gagcattaaa aaaaaatggc ttcaaattcc tgccagttac  | 1410 |
| acaaaactcc ttcccccag gcctgagaag ccatcagtat gtgattactg aagtaatggc   | 1470 |
| aggtgtagga tcaacaggtc cccaagatgt cattcctgcc cttttagaag ccctgttaca  | 1530 |
| tctccgaagt acattcattg tgtaactatt ttgactgact ttaaaaaacca atgctgtgaa | 1590 |
| aagcttcatt ccataaacat caacagtgag tgatttgtag atttacctta gccaaaatac  | 1650 |
| caatgctgga agcattgtgt ttgcattgaa gctgctgttc aacaagaaaa tttataaatt  | 1710 |
| tactaatgtc ttagcatggt aaagtttgca cattaacaga aattaagact gcaaagcagg  | 1770 |
|  |      |

| ttaaacttgc | ttctttataa | aacagatgtt | gggttaatag | catggtttac | tgtattaaag | 1830 |
|------------|------------|------------|------------|------------|------------|------|
| acttatacac | ccatttttaa | cctcattcag | acatcaagtt | atgtgtagct | tcacaatggt | 1890 |
| tcaagtggct | tacttcaaga | aatcttatac | ttgacagtac | accaatttta | ttgactaaaa | 1950 |
| atggatgaac | tttcctaaag | attcaaaggg | cccatcttag | tatcacgcag | ctgactgagc | 2010 |
| ccttcaaaac | tgacatctta | aggcccaatc | aagatccaca | tatcctgatt | ttgaactatg | 2070 |
| tgaaagtggg | actgttaagt | gcaagactaa | aataaattat | agcagacttt | ttagtaataa | 2130 |
| ctttccattt | tcaaacagta | tatcctgtgg | gccaaagggc | tatttcttaa | agaggcatgt | 2190 |
| aaatgtattt | atttatctaa | tgttttttc  | cccatgtaaa | cttgatatac | aaggtttagt | 2250 |
| atttgctcct | ctttcatatt | attttcacac | gtatactcag | atttggcatg | tacctttcaa | 2310 |
| catctccata | aaattaaaca | ccttttggag | aaaagatcca | ctattttctg | ctcaaaggtt | 2370 |
| tcgcctacct | aaagtggaac | atgttaaaaa | tctatgtgac | catcactgga | cagctttctc | 2430 |
| tcaaaacttt | ccttcaacgc | catggattag | caccagtttt | gtttacttta | aggtactttt | 2490 |
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⟨222⟩ (232)...(1083)

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gtcctgctca ggtgttaggt acagtgtgtt tgatcgtggt ggcttgaggg gaacccgctg 120
ttcagagctg tgactgcggc tgcactcaga gaagctgccc ttggctgctc gtagcgccgg 180

| gcct | tctc | tc c | tcgt | cato | a to | caga | gcag | cca | gtgt | ccg | ggag | gcag | gaa g | ate | ccc | 237 |
|------|------|------|------|------|------|------|------|-----|------|-----|------|------|-------|-----|-----|-----|
|      |      |      |      |      |      |      |      |     |      |     |      |      |       | Met | Pro |     |
|      |      |      |      |      |      |      |      |     |      |     |      |      |       | 1   | l   |     |
| cac  | tcc  | agc  | ctg  | cat  | cca  | tcc  | atc  | ccg | tgt  | ссс | agg  | ggt  | cac   | ggg | gcc | 285 |
| His  | Ser  | Ser  | Leu  | His  | Pro  | Ser  | Ile  | Pro | Cys  | Pro | Arg  | Gly  | His   | Gly | Ala |     |
|      |      | 5    |      |      |      |      | 10   |     |      |     |      | 15   |       |     |     |     |
| cag  | aag  | gca  | gcc  | ttg  | gtt  | ctg  | ctg  | agt | gcc  | tgc | ctg  | gtg  | acc   | ctt | tgg | 333 |
| Gln  | Lys  | Ala  | Ala  | Leu  | Val  | Leu  | Leu  | Ser | Ala  | Cys | Leu  | Val  | Thr   | Leu | Trp |     |
|      | 20   |      |      |      |      | 25   |      |     |      |     | 30   |      |       |     |     |     |
| ggg  | cta  | gga  | gag  | cca  | cca  | gag  | cac  | act | ctc  | cgg | tac  | ctg  | gtg   | ctc | cac | 381 |
| Gly  | Leu  | Gly  | Glu  | Pro  | Pro  | Glu  | His  | Thr | Leu  | Arg | Tyr  | Leu  | Val   | Leu | His |     |
| 35   |      |      |      |      | 40   |      |      |     |      | 45  |      |      |       |     | 50  |     |
| cta  | gcc  | tcc  | ctg  | cag  | ctg  | gga  | ctg  | ctg | tta  | aac | ggg  | gtc  | tgc   | agc | ctg | 429 |
| Leu  | Ala  | Ser  | Leu  | Gln  | Leu  | Gly  | Leu  | Leu | Leu  | Asn | Gly  | Val  | Cys   | Ser | Leu |     |
|      |      |      |      | 55   |      |      |      |     | 60   |     |      |      |       | 65  |     |     |
| gct  | gag  | gag  | ctg  | cac  | cac  | atc  | cac  | tcc | agg  | tac | cgg  | ggc  | agc   | tac | tgg | 477 |
| Ala  | Glu  | Glu  | Leu  | His  | His  | Ile  | His  | Ser | Arg  | Tyr | Arg  | Gly  | Ser   | Tyr | Trp |     |
|      |      |      | 70   |      |      |      |      | 75  |      |     |      |      | 80    |     |     |     |
| agg  | act  | gtg  | cgg  | gcc  | tgc  | ctg  | ggc  | tgc | ccc  | ctc | cgc  | cgt  | ggg   | gcc | ctg | 525 |
| Arg  | Thr  | Val  | Arg  | Ala  | Cys  | Leu  | Gly  | Cys | Pro  | Leu | Arg  | Arg  | Gly   | Ala | Leu |     |
|      |      | 85   |      |      |      |      | 90   |     |      |     |      | 95   |       |     |     |     |
| ttg  | ctg  | ctg  | tcc  | atc  | tat  | ttc  | tac  | tac | tcc  | ctc | cca  | aat  | gcg   | gtc | ggc | 573 |
| Leu  | Leu  | Leu  | Ser  | Ile  | Tyr  | Phe  | Tyr  | Tyr | Ser  | Leu | Pro  | Asn  | Ala   | Val | Gly |     |
|      | 100  |      |      |      |      | 105  |      |     | že.  |     | 110  |      |       |     |     |     |
| ccg  | ссс  | ttc  | act  | tgg  | atg  | ctt  | gcc  | ctc | ctg  | ggc | ctc  | tcg  | cag   | gca | ctg | 621 |

| Pro | Pro | Phe | Thr | Trp | Met | Leu | Ala | Leu | Leu | Gly   | Leu | Ser | Gln | Ala | Leu |      |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-------|-----|-----|-----|-----|-----|------|
| 115 |     |     |     |     | 120 |     |     |     |     | 125   |     |     |     |     | 130 |      |
| aac | atc | ctc | ctg | ggc | ctc | aag | ggc | ctg | gcc | cca   | gct | gag | atc | tct | gca | 669  |
| Asn | Ile | Leu | Leu | Gly | Leu | Lys | Gly | Leu | Ala | Pro   | Ala | Glu | Ile | Ser | Ala |      |
|     |     |     |     | 135 |     |     |     |     | 140 |       |     |     |     | 145 |     |      |
| gtg | tgt | gaa | aaa | ggg | aat | ttc | aac | gtg | gcc | cat   | ggg | ctg | gca | tgg | tca | 717  |
| Val | Cys | Glu | Lys | Gly | Asn | Phe | Asn | Val | Ala | His   | G1y | Leu | Ala | Trp | Ser |      |
|     |     |     | 150 |     |     |     |     | 155 |     |       |     |     | 160 |     |     |      |
| tat | tac | atc | gga | tat | ctg | cgg | ctg | atc | ctg | cca   | gag | ctc | cag | gcc | cgg | 765  |
| Tyr | Tyr | Ile | Gly | Tyr | Leu | Arg | Leu | Ile | Leu | Pro   | Glu | Leu | Gln | Ala | Arg |      |
|     |     | 165 |     |     |     |     | 170 |     |     |       |     | 175 |     |     |     |      |
| att | cga | act | tac | aat | cag | cat | tac | aac | aac | ctg   | cta | cgg | ggt | gca | gtg | 813  |
| Ile | Arg | Thr | Tyr | Asn | Gln | His | Tyr | Asn | Asn | Leu   | Leu | Arg | Gly | Ala | Val |      |
|     | 180 |     |     |     |     | 185 |     |     |     |       | 190 |     |     |     |     |      |
| agc | cag | cgg | ctg | tat | att | ctc | ctc | cca | ttg | gac   | tgt | ggg | gtg | cct | gat | 861  |
| Ser | Gln | Arg | Leu | Tyr | Ile | Leu | Leu | Pro | Leu | Asp   | Cys | Gly | Val | Pro | Asp |      |
| 195 |     |     |     |     | 200 |     |     |     |     | 205   |     |     |     |     | 210 |      |
| aac | ctg | agt | atg | gct | gac | ccc | aac | att | cgc | ttc   | ctg | gat | aaa | ctg | ccc | 909  |
| Asn | Leu | Ser | Met | Ala | Asp | Pro | Asn | Ile | Arg | Phe   | Leu | Asp | Lys | Leu | Pro |      |
|     |     |     |     | 215 |     |     |     |     | 220 |       |     |     |     | 225 |     |      |
| cag | cag | acc | gct | gac | cgt | gct | ggc | atc | aag | gat   | cgg | gtt | tac | agc | aac | 957  |
| Gln | Gln | Thr | Ala | Asp | Arg | Ala | Gly | Ile | Lys | Asp   | Arg | Val | Tyr | Ser | Asn | •    |
|     |     |     | 230 |     |     |     |     | 235 |     |       |     |     | 240 |     |     |      |
| agc | atc | tat | gag | ctt | ctg | gag | aac | ggg | cag | . cgg | aac | ctg | cag | atg | aca | 1005 |
| Ser | Ile | Tyr | Glu | Leu | Leu | Glu | Asn | Gly | Gln | Arg   | Asn | Leu | Gln | Met | Thr |      |

WO 01/12660 PCT/JP00/05356

## 194/307

| 245                    | 250              | 255                 |                 |
|------------------------|------------------|---------------------|-----------------|
| gca gct tct cgc tgt co | c agg agg ttc t  | cc ggc acc tgc ggc  | agg agg 1053    |
| Ala Ala Ser Arg Cys Pi | o Arg Arg Phe S  | er Gly Thr Cys Gly  | Arg Arg         |
| 260                    | 265              | 270                 |                 |
| aaa agg aag agg tta c  | tg tgg gca gct t | gaagacctc agcggtgco | cc 1100         |
| Lys Arg Lys Arg Leu Le | eu Trp Ala Ala   |                     |                 |
| 275 28                 | 30               |                     |                 |
| agtacctcca cgatgtccca  | agagcctgag ctcc  | tcatca gtggaatgga a | aaagcccctc 1160 |
| cctctccgca cggatttctc  | ttgagaccca gggt  | caccag gccagagcct   | ccagtggtct 1220 |
| ccaagcctct ggactggggg  | ctctcttcag tggc  | tgaatg tccagcagag ( | ctatttcctt 1280 |
| ccacaggggg ccttgcaggg  | aagggtccag gact  | tgacat cttaagatgc   | gtcttgtccc 1340 |
| cttgggccag tcatttcccc  | tctctgagcc tcgg  | tgtctt caacctgtga   | aatgggatca 1400 |
| taatcactgc cttacctccc  | tcacggttgt tgtg  | aggact gagtgtgtgg   | aagtttttca 1460 |
| taaactttgg atgctagtgt  | acttaggggg tgtg  | ccaggt gtctttcatg   | gggccttcca 1520 |
| gacccactcc ccacccttct  | cccttcctt tgcc   | egggga egeegaacte   | tctcaatggt 1580 |
| atcaacaggc tccttcgccc  | tctggctcct ggtc  | eatgttc cattattggg  | gagececage 1640 |
| agaagaatgg agaggaggag  | gaggctgagt ttg   | gggtatt gaatcccccg  | gctcccaccc 1700 |
| tgcagcatca aggttgctat  | ggactctcct gcc   | gggcaac tcttgcgtaa  | tcatgactat 1760 |
| ctctaggatt ctggcaccac  | ttccttccct ggc   | cccttaa gcctagctgt  | gtatcggcac 1820 |
| ccccacccca ctagagtact  | ccctctcact tgc   | ggtttcc ttatactcca  | ccctttctc 1880  |
| aacggtcctt ttttaaagca  | catctcagat t     |                     | 1911            |

<210> 91

<211> 476

<212> PRT

| <213> Homo sapiens |       |     |     |     |     |     |     |     |      |     |     |     |     |     |     |
|--------------------|-------|-----|-----|-----|-----|-----|-----|-----|------|-----|-----|-----|-----|-----|-----|
| <400               | )> 9: | l   |     |     |     |     |     |     |      |     |     |     |     |     |     |
| Met                | Val   | Gly | Ala | Met | Trp | Lys | Val | Ile | Val  | Ser | Leu | Val | Leu | Leu | Met |
| 1                  |       |     |     | 5   |     |     |     |     | 10   |     |     |     |     | 15  |     |
| Pro                | Gly   | Pro | Cys | Asp | Gly | Leu | Phe | Arg | Ser  | Leu | Tyr | Arg | Ser | Val | Ser |
|                    |       |     | 20  |     |     |     |     | 25  |      |     | •   |     | 30  |     |     |
| Met                | Pro   | Pro | Lys | Gly | Asp | Ser | Gly | Gln | Pro  | Leu | Phe | Leu | Thr | Pro | Tyr |
|                    |       | 35  |     |     |     |     | 40  |     |      |     |     | 45  |     |     |     |
| Ile                | Glu   | Ala | Gly | Lys | Ile | Gln | Lys | Gly | Arg  | Glu | Leu | Ser | Leu | Val | Gly |
|                    | 50    |     |     |     |     | 55  |     |     |      |     | 60  |     |     |     |     |
| Pro                | Phe   | Pro | Gly | Leu | Asn | Met | Lys | Ser | Tyr  | Ala | Gly | Phe | Leu | Thr | Val |
| 65                 |       |     |     |     | 70  | •   |     |     | -    | 75  |     |     |     |     | 80  |
| Asn                | Lys   | Thr | Tyr | Asn | Ser | Asn | Leu | Phe | Phe  | Trp | Phe | Phe | Pro | Ala | Gln |
|                    |       |     |     | 85  |     |     |     |     | 90   |     |     |     |     | 95  |     |
| Ile                | Gln   | Pro | Glu | Asp | Ala | Pro | Val | Val | Leu  | Trp | Leu | Gln | Gly | Gly | Pro |
|                    |       |     | 100 |     |     |     |     | 105 |      |     |     |     | 110 |     |     |
| Gly                | Gly   | Ser | Ser | Met | Phe | Gly | Leu | Phe | Val  | Glu | His | Gly | Pro | Tyr | Val |
|                    |       | 115 |     |     |     |     | 120 |     |      |     |     | 125 |     |     |     |
| Val                | Thr   | Ser | Asn | Met | Thr | Leu | Arg | Asp | Arg  | Asp | Phe | Pro | Trp | Thr | Thr |
|                    | 130   |     |     |     |     | 135 |     |     |      |     | 140 |     |     |     |     |
| Thr                | Leu   | Ser | Met | Leu | Tyr | Ile | Asp | Asn | Pro  | Val | Gly | Thr | Gly | Phe | Ser |
| 145                |       |     |     |     | 150 |     |     |     |      | 155 |     |     |     |     | 160 |
| Phe                | Thr   | Asp | Asp | Thr | His | Gly | Tyr | Ala | Val  | Asn | Glu | Asp | Asp | Val | Ala |
|                    |       |     |     | 165 |     | •   |     | /   | 1,70 |     |     |     |     | 175 |     |
| Arg                | Asp   | Leu | Tyr | Ser | Ala | Leu | Ile | Gln | Phe  | Phe | Gln | Ile | Phe | Pro | Glu |

|     |     |     | 180 |     |     |     |     | 185 |      |     |     |     | 190 |     |     |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|------|-----|-----|-----|-----|-----|-----|
| Tyr | Lys | Asn | Asn | Asp | Phe | Tyr | Val | Thr | Gly  | Glu | Ser | Tyr | Ala | Gly | Lys |
|     |     | 195 |     |     |     |     | 200 | •   |      |     |     | 205 |     |     |     |
| Tyr | Val | Pro | Ala | Ile | Ala | His | Leu | Ile | His  | Ser | Leu | Asn | Pro | Val | Arg |
|     | 210 |     |     |     |     | 215 |     |     |      |     | 220 |     |     |     |     |
| Glu | Val | Lys | Ile | Asn | Leu | Asn | Gly | Ile | Ala  | Ile | Gly | Asp | Gly | Tyr | Ser |
| 225 |     |     |     |     | 230 |     |     |     |      | 235 |     |     |     |     | 240 |
| Asp | Pro | Glu | Ser | Ile | Ile | Gly | Gly | Tyr | Ala  | Glu | Phe | Leu | Tyr | Gln | Ile |
|     |     |     |     | 245 |     |     |     |     | 250  |     |     |     |     | 255 |     |
| Gly | Leu | Leu | Asp | Glu | Lys | Gln | Lys | Lys | Tyr  | Phe | Gln | Lys | Gln | Cys | His |
|     |     |     | 260 |     |     |     |     | 265 |      |     |     |     | 270 |     |     |
| Glu | Cys | Ile | Glu | His | Ile | Arg | Lys | Gln | Asn  | Trp | Phe | Glu | Ala | Phe | Glu |
|     |     | 275 |     |     |     |     | 280 |     |      |     |     | 285 |     |     |     |
| Ile | Leu | Asp | Lys | Leu | Leu | Asp | Gly | Asp | Leu  | Thr | Ser | Asp | Pro | Ser | Tyr |
|     | 290 |     |     |     | •   | 295 |     |     |      |     | 300 |     |     |     |     |
| Phe | Gln | Asn | Val | Thr | Gly | Cys | Ser | Asn | Tyr  | Tyr | Asn | Phe | Leu | Arg | Cys |
| 305 |     |     |     |     | 310 |     |     |     |      | 315 |     |     |     |     | 320 |
| Thr | Glu | Pro | Glu | Asp | Gln | Leu | Tyr | Tyr | Val  | Lys | Phe | Leu | Ser | Leu | Pro |
|     |     |     |     | 325 |     |     |     |     | 330  |     |     |     |     | 335 |     |
| Glu | Val | Arg | Gln | Ala | Ile | His | Val | Gly | Asn  | Gln | Thr | Phe | Asn | Asp | Gly |
|     |     |     | 340 |     |     |     |     | 345 |      |     |     |     | 350 |     | •   |
| Thr | Ile | Val | Glu | Lys | Tyr | Leu | Arg | Glu | Asp  | Thr | Val | Gln | Ser | Val | Lys |
|     |     | 355 |     |     |     |     | 360 |     |      |     |     | 365 |     |     |     |
| Pro | Trp | Leu | Thr | Glu | Ile | Met | Asn | Asn | Tyr  | Lys | Val | Leu | Ile | Tyr | Asn |
|     | 370 |     |     |     |     | 375 |     | /   | نتمو |     | 380 |     |     |     |     |

Gly Gln Leu Asp Ile Ile Val Ala Ala Ala Leu Thr Glu His Ser Leu Met Gly Met Asp Trp Lys Gly Ser Gln Glu Tyr Lys Lys Ala Glu Lys Lys Val Trp Lys Ile Phe Lys Ser Asp Ser Glu Val Ala Gly Tyr Ile Arg Gln Ala Gly Asp Phe His Gln Val Ile Ile Arg Gly Gly Gly His Ile Leu Pro Tyr Asp Gln Pro Leu Arg Ala Phe Asp Met Ile Asn Arg Phe Ile Tyr Gly Lys Gly Trp Asp Pro Tyr Val Gly 5 <210> 92 <211> 226 <212> PRT <213> Homo sapiens <400> 92 Met Ser Arg Ala Gln Ile Trp Ala Leu Val Ser Gly Val Gly Gly Phe Gly Ala Leu Val Ala Ala Thr Thr Ser Asn Glu Trp Lys Val Thr Thr Arg Ala Ser Ser Val Ile Thr Ala Thr Trp Val Tyr Gln Gly Leu Trp Met Asn Cys Ala Gly Asn Ala Leu Gly Ser Phe His Cys Arg Pro His

|     | 50  |     |     |     |     | 55  |     |     |     |     | 60  |     |     |     |     |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
| Phe | Thr | Ile | Phe | Lys | Val | Ala | Gly | Tyr | Ile | Gln | Ala | Cys | Arg | Gly | Leu |
| 65  |     |     |     |     | 70  |     |     |     |     | 75  |     |     |     |     | 80  |
| Met | Ile | Ala | Ala | Val | Ser | Leu | Gly | Phe | Phe | Gly | Ser | Ile | Phe | Ala | Leu |
|     |     |     |     | 85  |     |     |     |     | 90  |     |     |     |     | 95  |     |
| Phe | Gly | Met | Lys | Cys | Thr | Lys | Val | Gly | Gly | Ser | Asp | Lys | Ala | Lys | Ala |
|     |     |     | 100 |     |     |     |     | 105 |     |     |     |     | 110 |     |     |
| Lys | Ile | Ala | Cys | Leu | Ala | Gly | Ile | Val | Phe | Ile | Leu | Ser | Gly | Leu | Cys |
|     |     | 115 |     |     |     |     | 120 |     |     |     |     | 125 |     |     |     |
| Ser | Met | Thr | Gly | Cys | Ser | Leu | Tyr | Ala | Asn | Lys | Ile | Thr | Thr | Glu | Phe |
|     | 130 |     |     |     |     | 135 |     |     |     |     | 140 |     |     |     |     |
| Phe | Asp | Pro | Leu | Phe | Val | Glu | Gln | Lys | Tyr | Glu | Leu | Gly | Ala | Ala | Leu |
| 145 |     |     |     |     | 150 |     |     |     |     | 155 |     |     |     |     | 160 |
| Phe | Ile | Gly | Trp | Ala | Gly | Ala | Ser | Leu | Cys | Ile | Ile | Gly | Gly | Val | Ile |
|     |     |     |     | 165 |     |     |     |     | 170 |     |     |     |     | 175 |     |
| Phe | Cys | Phe | Ser | Ile | Ser | Asp | Asn | Asn | Lys | Thr | Pro | Arg | Tyr | Thr | Tyr |
|     |     |     | 180 |     |     |     |     | 185 |     |     |     |     | 190 |     |     |
| Asn | Gly | Ala | Thr | Ser | Val | Met | Ser | Ser | Arg | Thr | Lys | Tyr | His | Gly | Gly |
| •   |     | 195 |     |     |     |     | 200 |     |     |     |     | 205 |     |     |     |
| Glu | Asp | Phe | Lys | Thr | Thr | Asn | Pro | Ser | Lys | Gln | Phe | Asp | Lys | Asn | Ala |
|     | 210 |     |     |     |     | 215 |     |     |     |     | 220 |     |     |     |     |
| Tyr | Val |     |     |     |     |     |     |     |     |     |     |     |     |     |     |
| 225 | ;   |     |     |     |     |     |     |     |     |     |     |     |     |     |     |

| <211 | > 30  | )5    |       |     |     |     |     |     |          |            |      |     |     |     |     |
|------|-------|-------|-------|-----|-----|-----|-----|-----|----------|------------|------|-----|-----|-----|-----|
| <212 | ?> PR | RT    |       |     |     |     |     |     |          |            |      |     |     |     |     |
| <213 | 8> Hc | omo s | sapie | ens |     |     |     |     |          |            |      |     |     |     |     |
| <400 | )> 93 | 3     |       |     |     |     |     |     |          |            |      |     |     |     |     |
| Met  | Gly   | Ile   | Gln   | Thr | Ser | Pro | Val | Leu | Leu      | Ala        | Ser  | Leu | Gly | Val | Gly |
| 1    |       |       |       | 5   |     |     |     |     | 10       |            |      |     |     | 15  |     |
| Leu  | Val   | Thr   | Leu   | Leu | Gly | Leu | Ala | Val | Gly      | Ser        | Tyr  | Leu | Val | Arg | Arg |
|      |       |       | 20    |     |     |     |     | 25  |          |            |      |     | 30  |     |     |
| Ser  | Arg   | Arg   | Pro   | Gln | Val | Thr | Leu | Leu | Asp      | Pro        | Asn  | Glu | Lys | Tyr | Leu |
|      |       | 35    |       |     |     |     | 40  |     |          |            |      | 45  |     |     |     |
| Leu  | Arg   | Leu   | Leu   | Asp | Lys | Thr | Thr | Val | Ser      | His        | Asn  | Thr | Lys | Arg | Phe |
|      | 50    |       |       |     |     | 55  |     |     |          |            | 60   |     |     |     |     |
| Arg  | Phe   | Ala   | Leu   | Pro | Thr | Ala | His | His | Thr      | Leu        | Gly  | Leu | Pro | Val | Gly |
| 65   |       |       |       |     | 70  |     |     |     |          | <b>7</b> 5 |      |     |     |     | 80  |
| Lys  | His   | Ile   | Tyr   | Leu | Ser | Thr | Arg | Ile | Asp      | Gly        | Ser  | Leu | Val | Ile | Arg |
|      |       |       |       | 85  |     |     |     |     | 90       |            |      |     |     | 95  |     |
| Pro  | Tyr   | Thr   | Pro   | Val | Thr | Ser | Asp | Glu | Asp      | Gln        | Gly  | Tyr | Val | Asp | Leu |
|      |       |       | 100   |     |     |     |     | 105 |          |            |      |     | 110 |     |     |
| Val  | Ile   | Lys   | Val   | Tyr | Leu | Lys | Gly | Val | His      | Pro        | Lys  | Phe | Pro | Glu | Gly |
|      |       | 115   |       |     |     |     | 120 |     |          |            |      | 125 |     |     |     |
| Gly  | Lys   | Met   | Ser   | Gln | Tyr | Leu | Asp | Ser | Leu      | Lys        | Val  | Gly | Asp | Val | Val |
|      | 130   |       |       |     |     | 135 |     |     |          |            | 140  |     |     |     |     |
| Glu  | Phe   | Arg   | G1y   | Pro | Ser | Gly | Leu | Leu | Thr      | Tyr        | Thr  | Gly | Lys | Gly | His |
| 145  |       |       |       |     | 150 |     |     | /   | ۵۰۰ متمق | 155        |      |     |     |     | 160 |
| Phe  | Asn   | Πla   | Gln   | Pro | Aen | Ive | Ive | Sar | Pro      | Pro        | G111 | Dro | Ara | Val | 416 |

<400> 94

#### 200/307

Lys Lys Leu Gly Met Ile Ala Gly Gly Thr Gly Ile Thr Pro Met Leu Gln Leu Ile Arg Ala Ile Leu Lys Val Pro Glu Asp Pro Thr Gln Cys Phe Leu Leu Phe Ala Asn Gln Thr Glu Lys Asp Ile Ile Leu Arg Glu Asp Leu Glu Glu Leu Gln Ala Arg Tyr Pro Asn Arg Phe Lys Leu Trp Phe Thr Leu Asp His Pro Pro Lys Asp Trp Ala Tyr Ser Lys Gly Phe Val Thr Ala Asp Met Ile Arg Glu His Leu Pro Ala Pro Gly Asp Asp Val Leu Val Leu Cys Gly Pro Pro Pro Met Val Gln Leu Ala Cys His Pro Asn Leu Asp Lys Leu Gly Tyr Ser Gln Lys Met Arg Phe Thr Tyr ⟨210⟩ 94 <211> 227 <212> PRT <213> Homo sapiens

| Met | Gly | пр  | ınr | met | Arg | Leu | vaı | lhr | Ala    | Ala | Leu | Leu | Leu | Gly | Leu   |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|--------|-----|-----|-----|-----|-----|-------|
| 1   |     |     |     | 5   |     |     |     |     | 10     |     |     |     |     | 15  |       |
| Met | Met | Val | Val | Thr | Gly | Asp | Glu | Asp | Glu    | Asn | Ser | Pro | Cys | Ala | His   |
|     |     |     | 20  |     |     |     |     | 25  |        |     |     |     | 30  |     |       |
| Glu | Ala | Leu | Leu | Asp | Glu | Asp | Thr | Leu | Phe    | Cys | Gln | Gly | Leu | Glu | Val   |
|     |     | 35  |     |     |     |     | 40  |     |        |     |     | 45  |     |     |       |
| Phe | Tyr | Pro | Glu | Leu | Gly | Asn | Ile | Gly | Cys    | Lys | Val | Val | Pro | Asp | Cys   |
|     | 50  |     |     |     |     | 55  |     |     |        |     | 60  |     |     |     |       |
| Asn | Asn | Tyr | Arg | Gln | Lys | Ile | Thr | Ser | Trp    | Met | Glu | Pro | Ile | Val | Lys   |
| 65  |     |     |     |     | 70  |     |     |     |        | 75  |     |     |     |     | 80    |
| Phe | Pro | Gly | Ala | Val | Asp | Gly | Ala | Thr | Tyr    | Ile | Leu | Val | Met | Val | Asp   |
|     |     |     |     | 85  |     |     |     |     | 90     |     |     |     |     | 95  |       |
| Pro | Asp | Ala | Pro | Ser | Arg | Ala | Glu | Pro | Arg    | Gln | Arg | Phe | Trp | Arg | His   |
|     |     |     | 100 |     |     |     |     | 105 |        |     |     |     | 110 |     |       |
| Trp | Leu | Val | Thr | Asp | Ile | Lys | Gly | Ala | Asp    | Leu | Lys | Lys | Gly | Lys | Ile   |
|     |     | 115 |     |     |     |     | 120 |     |        |     |     | 125 |     |     |       |
| G1n | Gly | Gln | Glu | Leu | Ser | Ala | Tyr | Gln | Ala    | Pro | Ser | Pro | Pro | Ala | His   |
|     | 130 |     |     |     |     | 135 |     |     |        |     | 140 |     |     |     |       |
| Ser | Gly | Phe | His | Arg | Tyr | G1n | Phe | Phe | Val    | Tyr | Leu | Gln | Glu | Gly | Lys   |
| 145 |     |     |     |     | 150 |     |     |     |        | 155 |     |     |     |     | 160   |
| Val | Ile | Ser | Leu | Leu | Pro | Lys | Glu | Asn | Lys    | Thr | Arg | Gly | Ser | Trp | Lys   |
|     |     |     |     | 165 |     |     |     |     | 170    |     |     |     |     | 175 |       |
| Met | Asp | Arg | Phe | Leu | Asn | Arg | Phe | His | Leu    | Gly | Glu | Pro | Glu | Ala | Ser   |
|     | •   |     | 180 |     |     |     |     | 185 | انتمو. | ••  |     |     | 190 |     |       |
| Thr | Gln | Phe | Met | Thr | Gln | Asn | Tur | Gln | Aen    | Sar | Pro | The | Lau | Cl. | A 1 - |

195 200 205 Pro Arg Glu Arg Ala Ser Glu Pro Lys His Lys Asn Gln Ala Glu Ile 220 210 . 215 Ala Ala Cys 225 ⟨210⟩ 95 <211> 441 <212> PRT <213> Homo sapiens <400> 95 Met Ala Ile His Lys Ala Leu Val Met Cys Leu Gly Leu Pro Leu Phe l 5 15 10 Leu Phe Pro Gly Ala Trp Ala Gln Gly His Val Pro Pro Gly Cys Ser 20 25 30 Gln Gly Leu Asn Pro Leu Tyr Tyr Asn Leu Cys Asp Arg Ser Gly Ala 35 40 45 Trp Gly Ile Val Leu Glu Ala Val Ala Gly Ala Gly Ile Val Thr Thr 50 55 60 Phe Val Leu Thr Ile Ile Leu Val Ala Ser Leu Pro Phe Val Gln Asp 70 75 65 80 Thr Lys Lys Arg Ser Leu Leu Gly Thr Gln Val Phe Phe Leu Leu Gly 85 90 95 Thr Leu Gly Leu Phe Cys Leu Val Phe Ala Cys Val Val Lys Pro Asp

105

110

100

| Phe | Ser | Thr | Cys | Ala | Ser | Arg | Arg | Phe  | Leu     | Phe | Gly | Val | Leu | Phe | Ala |
|-----|-----|-----|-----|-----|-----|-----|-----|------|---------|-----|-----|-----|-----|-----|-----|
|     |     | 115 |     |     |     |     | 120 |      |         |     |     | 125 |     |     |     |
| Ile | Cys | Phe | Ser | Cys | Leu | Ala | Ala | His  | Val     | Phe | Ala | Leu | Asn | Phe | Leu |
|     | 130 |     |     |     |     | 135 |     |      |         |     | 140 |     |     |     |     |
| Ala | Arg | Lys | Asn | His | Gly | Pro | Arg | Gly  | Trp     | Val | Ile | Phe | Thr | Val | Ala |
| 145 |     |     |     |     | 150 |     |     |      |         | 155 |     |     |     |     | 160 |
| Leu | Leu | Leu | Thr | Leu | Val | Glu | Val | .Ile | Ile     | Asn | Thr | Glu | Trp | Leu | Ile |
|     |     |     |     | 165 |     |     |     |      | 170     |     |     |     | •   | 175 |     |
| Ile | Thr | Leu | Val | Arg | Gly | Ser | Gly | Glu  | Gly     | Gly | Pro | Gln | Gly | Asn | Ser |
|     |     |     | 180 |     |     |     |     | 185  |         |     |     |     | 190 |     |     |
| Ser | Ala | Gly | Trp | Ala | Val | Ala | Ser | Pro  | Cys     | Ala | Ile | Ala | Asn | Met | Asp |
|     |     | 195 |     |     |     |     | 200 |      |         | •   |     | 205 |     |     |     |
| Phe | Val | Met | Λla | Leu | Ile | Tyr | Val | Met  | Leu     | Leu | Leu | Leu | Gly | Ala | Phe |
|     | 210 |     |     |     |     | 215 |     |      |         |     | 220 |     |     |     |     |
| Leu | Gly | Ala | Trp | Pro | Ala | Leu | Cys | Gly  | Arg     | Tyr | Lys | Arg | Trp | Arg | Lys |
| 225 |     |     |     |     | 230 |     |     |      |         | 235 |     |     |     |     | 240 |
| His | Gly | Val | Phe | Val | Leu | Leu | Thr | Thr  | Ala     | Thr | Ser | Val | Ala | Ile | Trp |
|     |     |     |     | 245 |     |     |     |      | 250     |     |     |     |     | 255 |     |
| Val | Val | Trp | Ile | Val | Met | Tyr | Thr | Tyr  | Gly     | Asn | Lys | Gln | His | Asn | Ser |
|     |     |     | 260 |     |     |     |     | 265  |         |     |     |     | 270 |     |     |
| Pro | Thr | Trp | Asp | Asp | Pro | Thr | Leu | Ala  | Ile     | Ala | Leu | Ala | Ala | Asn | Ala |
|     |     | 275 |     |     |     |     | 280 |      |         | •   |     | 285 |     |     |     |
| Trp | Ala | Phe | Val | Leu | Phe | Tyr | Val | Ile  | Pro     | Glu | Val | Ser | Gln | Val | Thr |
|     | 290 |     |     |     |     | 295 |     |      | • نشمو. |     | 300 |     |     |     |     |
| Lvs | Ser | Ser | Pro | Glu | Gln | Ser | Tvr | Gln  | Glv     | Asn | Met | Tur | Pro | Thr | Ara |

Gly Val Gly Tyr Glu Thr Ile Leu Lys Glu Gln Lys Gly Gln Ser Met Phe Val Glu Asn Lys Ala Phe Ser Met Asp Glu Pro Val Ala Ala Lys Arg Pro Val Ser Pro Tyr Ser Gly Tyr Asn Gly Gln Leu Leu Thr Ser Val Tyr Gln Pro Thr Glu Met Ala Leu Met His Lys Val Pro Ser Glu Gly Ala Tyr Asp Ile Ile Leu Pro Arg Ala Thr Ala Asn Ser Gln Val Met Gly Ser Ala Asn Ser Thr Leu Arg Ala Glu Asp Met Tyr Ser Ala Gln Ser His Gln Ala Ala Thr Pro Pro Lys Asp Gly Lys Asn Ser Gln Val Phe Arg Asn Pro Tyr Val Trp Asp 

<210> 96

<211> 265

<212> PRT

<213> Homo sapiens

<400> 96

Met Ala Ala Val Pro Lys Arg Met Arg Gly Pro Ala Gln Ala Lys

1 5 10 15

| Leu | Leu | Pro | GIY | Ser | Ala | He  | GIn | Ala | Leu    | Val | Gly | Leu | Ala | Arg | Pro |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|--------|-----|-----|-----|-----|-----|-----|
|     |     |     | 20  |     |     |     | •   | 25  |        |     |     |     | 30  |     |     |
| Leu | Val | Leu | Ala | Leu | Leu | Leu | Val | Ser | Ala    | Ala | Leu | Ser | Ser | Val | Val |
|     |     | 35  |     |     |     |     | 40  |     |        |     |     | 45  |     |     |     |
| Ser | Arg | Thr | Asp | Ser | Pro | Ser | Pro | Thr | Val    | Leu | Asn | Ser | His | Ile | Ser |
|     | 50  |     |     |     |     | 55  |     |     |        |     | 60  |     |     |     |     |
| Thr | Pro | Asn | Val | Asn | Ala | Leu | Thr | His | Glu    | Asn | Gln | Thr | Lys | Pro | Ser |
| 65  |     |     |     |     | 70  |     |     |     |        | 75  |     |     |     |     | 80  |
| Ile | Ser | Gln | Ile | Ser | Thr | Thr | Leu | Pro | Pro    | Thr | Thr | Ser | Thr | Lys | Lys |
|     |     |     |     | 85  |     |     |     |     | 90     |     |     |     |     | 95  |     |
| Ser | Gly | Gly | Ala | Ser | Val | Val | Pro | His | Pro    | Ser | Pro | Thr | Pro | Leu | Ser |
|     |     |     | 100 |     |     |     |     | 105 |        |     |     |     | 110 |     |     |
| Gln | Glu | Glu | Ala | Asp | Asn | Asn | Glu | Asp | Pro    | Ser | He  | Glu | Glu | Glu | Asp |
|     |     | 115 |     |     |     |     | 120 |     |        |     |     | 125 |     |     |     |
| Leu | Leu | Met | Leu | Asn | Ser | Ser | Pro | Ser | Thr    | Ala | Lys | Asp | Thr | Leu | Asp |
|     | 130 |     |     |     |     | 135 |     |     |        |     | 140 |     |     |     |     |
| Asn | Gly | Asp | Tyr | Gly | Glu | Pro | Asp | Tyr | Asp    | Trp | Thr | Thr | Gly | Pro | Arg |
| 145 |     |     |     |     | 150 |     |     |     |        | 155 |     |     |     |     | 160 |
| Asp | Asp | Asp | Glu | Ser | Asp | Asp | Thr | Leu | Glu    | Glu | Asn | Arg | Gly | Tyr | Met |
|     |     |     |     | 165 |     |     |     |     | 170    |     |     |     |     | 175 |     |
| Glu | Ile | Glu | Gln | Ser | Val | Lys | Ser | Phe | Lys    | Met | Pro | Ser | Ser | Asn | He  |
|     |     |     | 180 |     |     |     |     | 185 |        |     |     |     | 190 |     |     |
| Glu | Glu | Glu | Asp | Ser | His | Phe | Phe | Phe | His    | Leu | Ile | Ile | Phe | Ala | Phe |
|     |     | 195 |     |     |     |     | 200 |     | انتشو. | ••  |     | 205 |     |     |     |
| Cys | Ile | Ala | Val | Val | Tyr | Ile | Thr | Tyr | His    | Asn | Lys | Arg | Lys | Ile | Phe |

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206/307

⟨210⟩ 97

<211> 208

<212> PRT

<213> Homo sapiens

<400> 97

Met Leu Gly Leu Leu Val Ala Leu Leu Ala Leu Gly Leu Ala Val Phe

1 5 10 15

Ala Leu Leu Asp Val Trp Tyr Leu Val Arg Leu Pro Cys Ala Val Leu
20 25 30

Arg Ala Arg Leu Leu Gln Pro Arg Val Arg Asp Leu Leu Ala Glu Gln
35 40 45

Arg Phe Pro Gly Arg Val Leu Pro Ser Asp Leu Asp Leu Leu Leu His
50 55 60

Met Asn Asn Ala Arg Tyr Leu Arg Glu Ala Asp Phe Ala Arg Val Ala
65 70 75 80

His Leu Thr Arg Cys Gly Val Leu Gly Ala Leu Arg Glu Leu Arg Ala

85 / 90 95

His Thr Val Leu Ala Ala Ser Cys Ala Arg His Arg Arg Ser Leu Arg Leu Leu Glu Pro Phe Glu Val Arg Thr Arg Leu Leu Gly Trp Asp Asp Arg Ala Phe Tyr Leu Glu Ala Arg Phe Val Ser Leu Arg Asp Gly Phe Val Cys Ala Leu Leu Arg Phe Arg Gln His Leu Leu Gly Thr Ser Pro Glu Arg Val Val Gln His Leu Cys Gln Arg Arg Val Glu Pro Pro Glu Leu Pro Ala Asp Leu Gln His Trp Ile Ser Tyr Asn Glu Ala Ser Ser Gln Leu Leu Arg Met Glu Ser Gly Leu Ser Asp Val Thr Lys Asp Gln <210> 98 <211> 400 <212> PRT <213> Homo sapiens <400> 98 Met Ala Trp Arg Arg Glu Ala Ser Val Gly Ala Arg Gly Val Leu Ala Leu Ala Leu Leu Ala Leu Ala Leu Cys Val Pro Gly Ala Arg Gly Arg Ala Leu Glu Trp Phe Ser Ala Val Val Asn Ile Glu Tyr Val Asp

|            |     | 35  |     |     |     |      | 40  |     |            |     |     | 45  |     |     |     |
|------------|-----|-----|-----|-----|-----|------|-----|-----|------------|-----|-----|-----|-----|-----|-----|
| Pro        | Gln | Thr | Asn | Leu | Thr | Val  | Trp | Ser | Val        | Ser | Glu | Ser | Gly | Arg | Phe |
|            | 50  |     |     |     |     | 55   |     |     |            |     | 60  |     |     |     |     |
| Gly        | Asp | Ser | Ser | Pro | Lys | Glu  | Gly | Ala | His        | Gly | Leu | Val | Gly | Val | Pro |
| <b>6</b> 5 |     |     |     |     | 70  |      |     |     |            | 75  |     |     |     |     | 80  |
| Trp        | Ala | Pro | Gly | Gly | Asp | Leu  | Glu | Gly | Cys        | Ala | Pro | Asp | Thr | Arg | Phe |
|            |     |     |     | 85  |     |      |     |     | 90         |     |     |     |     | 95  |     |
| Phe        | Val | Pro | Glu | Pro | Gly | Gly  | Arg | Gly | Ala        | Ala | Pro | Trp | Val | Ala | Leu |
|            |     |     | 100 |     |     |      |     | 105 |            |     |     |     | 110 |     |     |
| Val        | Ala | Arg | Gly | Gly | Cys | Thr  | Phe | Lys | Asp        | Lys | Val | Leu | Val | Ala | Ala |
|            |     | 115 |     |     |     |      | 120 |     |            |     |     | 125 |     |     |     |
| Arg        | Arg | Asn | Ala | Ser | Ala | Val  | Val | Leu | Tyr        | Asn | Glu | Glu | Arg | Tyr | Gly |
|            | 130 |     |     |     |     | 135  |     |     |            |     | 140 |     |     |     |     |
| Asn        | He  | Thr | Leu | Pro | Met | Ser  | His | Ala | Gly        | Thr | Gly | Asn | Ile | Val | Val |
| 145        |     |     |     |     | 150 |      |     |     |            | 155 |     |     |     |     | 160 |
| Ile        | Met | Ile | Ser | Tyr | Pro | Lys  | Gly | Arg | Glu        | Ile | Leu | Glu | Leu | Val | Gln |
|            |     |     |     | 165 |     |      |     |     | 170        |     |     |     |     | 175 |     |
| Lys        | Gly | Ile | Pro | Val | Thr | Met. | Thr | Ile | Gly        | Val | Gly | Thr | Arg | His | Val |
|            |     |     | 180 |     |     |      |     | 185 |            |     | •   |     | 190 |     |     |
| Gln        | Glu | Phe | Ile | Ser | Gly | Gln  | Ser | Val | Val        | Phe | Val | Ala | Ile | Ala | Phe |
|            |     | 195 |     |     |     |      | 200 |     |            |     |     | 205 |     |     |     |
| Ile        | Thr | Met | Met | Ile | Ile | Ser  | Leu | Ala | Trp        | Leu | He  | Phe | Tyr | Tyr | Ile |
|            | 210 |     |     |     |     | 215  |     |     |            |     | 220 |     |     |     |     |
| Gln        | Arg | Phe | Leu | Tyr | Thr | Gly  | Ser | Gln | Ile<br>نىر | Gly | Ser | Gln | Ser | His | Arg |
| 225        |     |     |     |     | 230 |      |     | /   |            | 235 |     |     |     |     | 240 |

Lys Glu Thr Lys Lys Val Ile Gly Gln Leu Leu His Thr Val Lys His Gly Glu Lys Gly Ile Asp Val Asp Ala Glu Asn Cys Ala Val Cys Ile Glu Asn Phe Lys Val Lys Asp Ile Ile Arg Ile Leu Pro Cys Lys His Ile Phe His Arg Ile Cys Ile Asp Pro Trp Leu Leu Asp His Arg Thr Cys Pro Met Cys Lys Leu Asp Val Ile Lys Ala Leu Gly Tyr Trp Gly Glu Pro Gly Asp Val Gln Glu Met Pro Ala Pro Glu Ser Pro Pro Gly Arg Asp Pro Ala Ala Asn Leu Ser Leu Ala Leu Pro Asp Asp Asp Gly Ser Asp Glu Ser Ser Pro Pro Ser Ala Ser Pro Ala Glu Ser Glu Pro Gln Cys Asp Pro Ser Phe Lys Gly Asp Ala Gly Glu Asn Thr Ala Leu Leu Glu Ala Gly Arg Ser Asp Ser Arg His Gly Gly Pro Ile Ser 

<210> 99

<211> 192

<212> PRT

<213> Homo sapiens

| <400 | )> 99 | 9   |     |     |     |     |     |     |     |     |     |     |     |     |     |
|------|-------|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
| Met  | Phe   | Cys | Pro | Leu | Lys | Leu | He  | Leu | Leu | Pro | Val | Leu | Leu | Asp | Tyr |
| 1    |       |     |     | 5   |     |     |     |     | 10  |     |     |     |     | 15  |     |
| Ser  | Leu   | Gly | Leu | Asn | Asp | Leu | Asn | Val | Ser | Pro | Pro | Glu | Leu | Thr | Val |
|      |       |     | 20  |     |     |     |     | 25  |     |     |     |     | 30  |     |     |
| His  | Val   | Gly | Asp | Ser | Ala | Leu | Met | Gly | Cys | Val | Phe | Gln | Ser | Thr | Glu |
|      |       | 35  |     |     |     |     | 40  |     |     |     |     | 45  |     |     |     |
| Лsp  | Lys   | Cys | Ile | Phe | Lys | Ile | Asp | Trp | Thr | Leu | Ser | Pro | Gly | Glu | His |
|      | 50    |     |     |     |     | 55  |     |     |     |     | 60  |     |     |     |     |
| Ala  | Lys   | Asp | Glu | Tyr | Val | Leu | Tyr | Tyr | Tyr | Ser | Asn | Leu | Ser | Val | Pro |
| 65   |       |     |     |     | 70  |     |     |     |     | 75  |     |     |     |     | 80  |
| He   | Gly   | Λrg | Phe | Gln | Asn | Arg | Val | His | Leu | Met | Gly | Asp | Asn | Leu | Cys |
|      |       |     |     | 85  |     |     |     |     | 90  |     |     |     |     | 95  |     |
| Asn  | Asp   | Gly | Ser | Leu | Leu | Leu | Gln | Asp | Val | Gln | Glu | Ala | Asp | Gln | Gly |
|      |       |     | 100 |     |     |     |     | 105 |     |     |     |     | 110 |     |     |
| Thr  | Tyr   | Ile | Cys | Glu | Ile | Arg | Leu | Lys | Gly | Glu | Ser | Gln | Val | Phe | Lys |
|      |       | 115 |     |     |     |     | 120 |     |     |     |     | 125 |     |     |     |
| Lys  | Ala   | Val | Val | Leu | His | Val | Leu | Pro | Glu | Glu | Pro | Lys | Glu | Leu | Met |
|      | 130   |     |     |     |     | 135 |     |     |     |     | 140 |     |     |     |     |
| Val  | His   | Val | Gly | Gly | Leu | Ile | Gln | Met | Gly | Cys | Val | Phe | Gln | Ser | Thr |
| 145  |       |     |     |     | 150 |     |     |     |     | 155 |     |     |     |     | 160 |
| Glu  | Val   | Lys | His | Val | Thr | Lys | Val | Glu | Trp | Ile | Phe | Ser | Gly | Arg | Arg |
|      |       |     |     | 165 |     |     |     |     | 170 |     |     |     |     | 175 |     |
| Ala  | Lys   | Val | Thr | Arg | Arg | Lys | His | His | Cys | Val | Arg | Glu | Gly | Ser | Gly |

185

190

180

| .<21 | 0> 1 | 00  |      |     |     |     |     |     |         |     |     |     |     |      |     |
|------|------|-----|------|-----|-----|-----|-----|-----|---------|-----|-----|-----|-----|------|-----|
| <21  | 1> 2 | 60  |      |     |     |     |     |     |         |     |     |     |     |      |     |
| <21  | 2> P | RT  |      |     |     |     |     |     |         |     |     |     |     |      |     |
| <21  | 3> H | omo | sapi | ens |     |     |     |     |         |     |     |     |     |      |     |
| <40  | 0> 1 | 00  |      |     |     |     |     |     |         |     |     |     |     |      |     |
| Met  | Ala  | G1y | Ser  | Pro | Leu | Leu | Trp | Gly | Pro     | Arg | Ala | Gly | Gly | Val  | Gly |
| 1    |      |     |      | 5   |     |     |     |     | 10      |     |     |     |     | . 15 |     |
| Leu  | Leu  | Val | Leu  | Leu | Leu | Leu | Gly | Leu | Phe     | Arg | Pro | Pro | Pro | Ala  | Leu |
|      |      |     | 20   |     |     |     |     | 25  |         |     |     |     | 30  |      |     |
| Cys  | Ala  | Arg | Pro  | Val | Lys | Glu | Pro | Arg | Gly     | Leu | Ser | Ala | Ala | Ser  | Pro |
|      |      | 35  |      |     |     |     | 40  |     |         |     |     | 45  |     |      |     |
| Pro  | Leu  | Ala | Glu  | Thr | Gly | Ala | Pro | Arg | Arg     | Phe | Arg | Arg | Ser | Val  | Pro |
|      | 50   |     |      |     |     | 55  |     |     |         |     | 60  |     |     |      |     |
| Arg  | Gly  | Glu | Ala  | Ala | Gly | Ala | Val | Gln | Glu     | Leu | Ala | Arg | Ala | Leu  | Ala |
| 65   |      |     |      |     | 70  |     |     |     |         | 75  |     |     |     |      | 80  |
| His  | Leu  | Leu | Glu  | Ala | Glu | Arg | Gln | Glu | Arg     | Ala | Arg | Ala | Glu | Ala  | G1n |
|      |      |     |      | 85  |     |     |     |     | 90      |     |     |     |     | 95   |     |
| Glu  | Ala  | Glu | Asp  | Gln | Gln | Ala | Arg | Val | Leu     | Ala | Gln | Leu | Leu | Arg  | Val |
|      |      |     | 100  |     |     |     |     | 105 |         |     |     |     | 110 |      |     |
| Trp  | Gly  | Ala | Pro  | Arg | Asn | Ser | Asp | Pro | Ala     | Leu | Gly | Leu | Asp | Asp  | Asp |
|      |      | 115 |      |     |     |     | 120 |     |         |     |     | 125 |     |      |     |
| Pro  | Asp  | Ala | Pro  | Ala | Ala | Gln | Leu | Ala | Arg     | Ala | Leu | Leu | Arg | Ala  | Arg |
|      | 130  |     |      |     |     | 135 |     |     | ۰۰ ننمو |     | 140 |     |     |      |     |
| Leu  | Asp  | Pro | Ala  | Ala | Leu | Ala | Ala | Gln | Leu     | Val | Pro | Ala | Pro | Val  | Pro |

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Ala Ala Ala Leu Arg Pro Arg Pro Pro Val Tyr Asp Asp Gly Pro Ala Gly Pro Asp Ala Glu Glu Ala Gly Asp Glu Thr Pro Asp Val Asp Pro Glu Leu Leu Arg Tyr Leu Leu Gly Arg Ile Leu Ala Gly Ser Ala Asp Ser Glu Gly Val Ala Ala Pro Arg Arg Leu Arg Arg Ala Ala Asp His Asp Val Gly Ser Glu Leu Pro Pro Glu Gly Val Leu Gly Ala Leu Leu Arg Val Lys Arg Leu Glu Thr Pro Ala Pro Gln Val Pro Ala Arg Arg Leu Leu Pro Pro

<210> 101

⟨211⟩ 1428

<212> DNA

<213> Homo sapiens

<400> 101

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| aataagactt | acaacagcaa | cctcttcttc | tggttcttcc | cagctcagat | acagccagaa | 300  |
|------------|------------|------------|------------|------------|------------|------|
| gatgccccag | tagttctctg | gctacagggt | gggccgggag | gttcatccat | gtttggactc | 360  |
| tttgtggaac | atgggcctta | tgttgtcaca | agtaacatga | ccttgcgtga | cagagacttc | 420  |
| ccctggacca | caacgctctc | catgctttac | attgacaatc | cagtgggcac | aggcttcagt | 480  |
| tttactgatg | atacccacgg | atatgcagtc | aatgaggacg | atgtagcacg | ggatttatac | 540  |
| agtgcactaa | ttcagttttt | ccagatattt | cctgaatata | aaaataatga | cttttatgtc | 600  |
| actggggagt | cttatgcagg | gaaatatgtg | ccagccattg | cacacctcat | ccattccctc | 660  |
| aaccctgtga | gagaggtgaa | gatcaacctg | aacggaattg | ctattggaga | tggatattct | 720  |
| gatcccgaat | caattatagg | gggctatgca | gaattcctgt | accaaattgg | cttgttggat | 780  |
| gagaagcaaa | aaaagtactt | ccagaagcag | tgccatgaat | gcatagaaca | catcaggaag | 840  |
| cagaactggt | ttgaggcctt | tgaaatactg | gataaactac | tagatggcga | cttaacaagt | 900  |
| gateettett | acttccagaa | tgttacagga | tgtagtaatt | actataactt | tttgcggtgc | 960  |
| acggaacctg | aggatcagct | ttactatgtg | aaatttttgt | cacteceaga | ggtgagacaa | 1020 |
| gccatccacg | tggggaatca | gacttttaat | gatggaacta | tagttgaaaa | gtacttgcga | 1080 |
| gaagatacag | tacagtcagt | taagccatgg | ttaactgaaa | tcatgaataa | ttataaggtt | 1140 |
| ctgatctaca | atggccaact | ggacatcatc | gtggcagctg | ccctgacaga | gcactccttg | 1200 |
| atgggcatgg | actggaaagg | atcccaggaa | tacaagaagg | cagaaaaaaa | agtttggaag | 1260 |
| atctttaaat | ctgacagtga | agtggctggt | tacatccggc | aagcgggtga | cttccatcag | 1320 |
| gtaattattc | gaggtggagg | acatatttta | ccctatgacc | agcctctgag | agcttttgac | 1380 |
| atgattaatc | gattcattta | tggaaaagga | tgggatcctt | atgttgga   |            | 1428 |

<210> 102

<211> 678

<212> DNA

<213> Homo sapiens

<400> 102

| atgtccaggg | cgcagatctg | ggctctggtg | tctggtgtcg | gagggtttgg | agctctcgtt | 60  |
|------------|------------|------------|------------|------------|------------|-----|
| gctgctacca | cgtccaatga | gtggaaagtg | accacgcgag | cctcctcggt | gataacagcc | 120 |
| acttgggttt | accagggtct | gtggatgaac | tgcgcaggta | acgcgttggg | ttctttccat | 180 |
| tgccgaccgc | attttactat | cttcaaagta | gcaggttata | tacaggcatg | tagaggactt | 240 |
| atgatcgctg | ctgtcagcct | gggcttcttt | ggttccatat | ttgcgctctt | tggaatgaag | 300 |
| tgtaccaaag | tcggaggctc | cgataaagcc | aaagctaaaa | ttgcttgttt | ggctgggatt | 360 |
| gtattcatac | tgtcagggct | gtgctcaatg | actggatgtt | ccctatatgc | aaacaaaatc | 420 |
| acaacggaat | tctttgatcc | tctctttgtt | gagcaaaagt | atgaattagg | agccgctctg | 480 |
| tttattggat | gggcaggagc | ctcactgtgc | ataattggtg | gtgtcatatt | ttgcttttca | 540 |
| atatctgaca | acaacaaaac | acccagatac | acatacaacg | gggccacatc | tgtcatgtct | 600 |
| teteggacaa | agtatcatgg | tggagaagat | tttaaaacaa | caaacccttc | aaaacagttt | 660 |
| gataaaaatg | cttatgtc   |            |            |            |            | 678 |

<210> 103

<211> 915

<212> DNA

<213> Homo sapiens

<400> 103

atggggatcc agacgagccc cgtcctgctg gcctccctgg gggtggggct ggtcactctg 60 ctcggcctgg ctgtgggct ctacttggtt cggaggtccc gccggcctca ggtcactctc 120 ctggacccca atgaaaagta cctgctacga ctgctagaca agacgactgt gagccacaac 180 accaagaggt tccgctttgc cctgcccacc gcccaccaca ctctggggct gcctgtgggc 240 aaacatatct acctctcac ccgaattgat ggcagcctgg tcatcaggcc atacactcct 300 gtcaccagtg atgaggatca aggctatgtg gátcttgtca tcaaggtcta cctgaagggt 360

| gtgcacccca | aatttcctga | gggagggaag | atgtctcagt | acctggatag | cctgaaggtt  | 420 |
|------------|------------|------------|------------|------------|-------------|-----|
| ggggatgtgg | tggagtttcg | ggggccaagc | gggttgctca | cttacactgg | aaaagggcat  | 480 |
| tttaacattc | agcccaacaa | gaaatctcca | ccagaacccc | gagtggcgaa | gaaactggga  | 540 |
| atgattgccg | gcgggacagg | aatcacccca | atgctacagc | tgatccgggc | catcctgaaa  | 600 |
| gtccctgaag | atccaaccca | gtgctttctg | ctttttgcca | accagacaga | aaaggatatc  | 660 |
| atcttgcggg | aggacttaga | ggaactgcag | gcccgctatc | ccaatcgctt | taagctctgg  | 720 |
| ttcactctgg | atcatcccc  | aaaagattgg | gcctacagca | agggctttgt | gactgccgac  | 780 |
| atgatccggg | aacacctgcc | cgctccaggg | gatgatgtgc | tggtactgct | ttgtgggcca  | 840 |
| ccccaatgg  | tgcagctggc | ctgccatccc | aacttggaca | aactgggcta | ctcacaaaaag | 900 |
| atgcgattca | cctac      |            |            |            |             | 915 |

<210> 104

<211> 681

<212> DNA

<213> Homo sapiens

<400> 104

atgggttgga caatgaggct ggtcacagca gcactgttac tgggtctcat gatggtggtc 60 actggagacg aggatgagaa cagcccgtgt gcccatgagg ccctcttgga cgaggacacc 120 ctcttttgcc agggccttga agttttctac ccagagttgg ggaacattgg ctgcaaggtt 180 gttcctgatt gtaacaacta cagacagaag atcacctcct ggatggagcc gatagtcaag 240 ttcccggggg ccgtggacgg cgcaacctat atcctggtga tggtggatcc agatgcccct 300 agcagagcag aacccagaca gagattctgg agacattggc tggtaacaga tatcaagggc 360 gccgacctga agaaagggaa gattcagggc caggagttat cagcctacca ggctcctcc 420 ccaccggcac acagtggctt ccatcgctac cagttctttg tctatcttca ggaaggaaaa 480 gtcatctctc tccttcccaa ggaaaacaaa actcgaggct cttggaaaat ggacagattt 540

| ctgaaccgtt | tccacctggg | cgaacctgaa | gcaagcaccc | agttcatgac | ccagaactac | 600 |
|------------|------------|------------|------------|------------|------------|-----|
| caggactcac | caaccctcca | ggctcccaga | gaaagggcca | gcgagcccaa | gcacaaaaac | 660 |
| caggcggaga | tagctgcctg | С          |            |            |            | 681 |

<210> 105

⟨211⟩ 1323

<212> DNA

<213> Homo sapiens

⟨400⟩ 105

atggccatcc acaaagcctt ggtgatgtgc ctgggactgc ctctcttcct gttcccaggg 60 gcctgggccc agggccatgt cccacccggc tgcagccaag gcctcaaccc cctgtactac 120 aacctgtgtg accgctctgg ggcgtgggc atcgtcctgg aggccgtggc tgggggggc 180 attgtcacca cgtttgtgct caccatcatc ctggtggcca gcctcccctt tgtgcaggac 240 accaagaaac ggagcctgct ggggacccag gtattcttcc ttctggggac cctgggcctc 300 ttctgcctcg tgtttgcctg tgtggtgaag cccgacttct ccacctgtgc ctctcggcgc 360 420 tteetetttg gggttetgtt egecatetge ttetettgte tggeggetea egtetttgee ctcaacttcc tggcccggaa gaaccacggg ccccggggct gggtgatctt cactgtggct 480 ctgctgctga ccctggtaga ggtcatcatc aatacagagt ggctgatcat caccctggtt 540 cggggcagtg gcgagggcgg ccctcagggc aacagcagcg caggctgggc cgtggcctcc 600 ccctgtgcca tcgccaacat ggactttgtc atggcactca tctacgtcat gctgctgctg 660 ctgggtgcct tcctgggggc ctggcccgcc ctgtgtggcc gctacaagcg ctggcgtaag 720 catggggtct ttgtgctcct caccacagcc acctccgttg ccatatgggt ggtgtggatc 780 840 gtcatgtata cttacggcaa caagcagcac aacagtccca cctgggatga ccccacgctg 900 gecategeee tegeogecaa tgeetgggee ttegteetet tetaegteat eecegaggte tcccaggtga ccaagtccag cccagagcaa agctaccagg gggacatgta ccccacccgg 960

| ggcgtgggct | atgagaccat | cctgaaagag | cagaagggtc | agagcatgtt | cgtggagaac | 1020 |
|------------|------------|------------|------------|------------|------------|------|
| aaggcctttt | ccatggatga | gccggttgca | gctaagaggc | cggtgtcacc | atacagcggg | 1080 |
| tacaatgggc | agctgctgac | cagtgtgtac | cagcccactg | agatggccct | gatgcacaaa | 1140 |
| gttccgtccg | aaggagctta | cgacatcatc | ctcccacggg | ccaccgccaa | cagccaggtg | 1200 |
| atgggcagtg | ccaactcgac | cctgcgggct | gaagacatgt | actcggccca | gagccaccag | 1260 |
| gcggccacac | cgccgaaaga | cggcaagaac | tctcaggtct | ttagaaaccc | ctacgtgtgg | 1320 |
| gac        |            |            |            |            |            | 1323 |

<210> 106

<211> 795

<212> DNA

<213> Homo sapiens

<400> 106

atggccgctg ccgtcccgaa gaggatgagg gggccagcac aagcgaaact gctgcccggg 60 teggecatee aageeettgt ggggttggeg eggeegetgg tettggeget eetgettgtg 120 teegeegete tateeagtgt tgtateaegg actgatteae egageecaae egtaeteaae 180 tcacatattt ctaccccaaa tgtgaatgct ttaacacatg aaaaccaaac caaaccttct 240 atttcccaaa tcagcaccac cctccctccc acgacgagta ccaagaaaag tggaggagca 300 tetgtggtcc ctcatccctc gcctactcct ctgtctcaag aggaagctga taacaatgaa 360 gatcctagta tagaggagga ggatcttctc atgctgaaca gttctccatc cacagccaaa 420 gacactctag acaatggcga ttatggagaa ccagactatg actggaccac gggccccagg 480 gacgacgacg agtctgatga caccttggaa gaaaacaggg gttacatgga aattgaacag 540 tcagtgaaat cttttaagat gccatcctca aatatagaag aggaagacag ccatttcttt 600 tttcatctta ttatttttgc tttttgcatt gctgttgttt acattacata tcacaacaaa 660 aggaagattt ttcttctggt tcaaagcagg aaatggcgtg atggcctttg ttccaaaaca 720

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| gtggaatacc | atcgcctaga | tcagaatgtt | aatgaggcaa | tgccttcttt | gaagattacc | 780 |
|------------|------------|------------|------------|------------|------------|-----|
| aatgattata | ttttt      |            |            |            |            | 795 |
|            |            |            |            |            |            |     |
| <210> 107  |            |            |            |            |            |     |
| <211> 624  |            |            |            |            |            |     |
| <212> DNA  |            |            |            |            |            |     |
| <213> Homo | sapiens    |            |            |            |            |     |
| <400> 107  |            |            |            |            |            |     |
| atgctggggc | tgctggtggc | gttgctggcc | ctggggctcg | ctgtctttgc | gctgctggac | 60  |
| gtctggtacc | tggtgcgcct | tccgtgcgcc | gtgctgcgcg | cgcgcctgct | gcagccgcgc | 120 |
| gtccgtgacc | tgctagctga | gcagcgcttc | ccgggccgcg | tgctgccctc | ggacttggac | 180 |
| ctgctgttgc | acatgaacaa | cgcgcgctac | ctgcgcgagg | ccgactttgc | gcgcgtcgcg | 240 |
| cacctgaccc | gctgcggggt | gctcggggcg | ctgagggagt | tgcgggcgca | cacggtgctg | 300 |
| gcggcctcgt | gcgcgcgcca | ccgccgctcg | ctgcgcctgc | tggagccctt | cgaggtgcgc | 360 |
| acccgcctgc | tgggctggga | cgaccgcgcg | ttctacctgg | aggcgcgctt | tgtcagcctg | 420 |
| cgggacggtt | tcgtgtgcgc | gctgctgcgc | ttccggcagc | acctgctggg | cacctcaccc | 480 |
| gagcgcgtcg | tgcagcacct | gtgccagcgc | agggtggagc | cccctgagct | gcccgctgat | 540 |
| ctgcagcact | ggatctccta | caacgaggcc | agcagccagc | tgctccgcat | ggagagtggg | 600 |
| ctcagtgatg | tcaccaagga | ccag       |            | _          |            | 624 |
|            |            |            |            |            |            |     |

⟨210⟩ 108

<211> 1200

<212> DNA

<213> Homo sapiens

<400> 108

| 60   | tctggcgttg | gcgtgttggc | ggggctcgcg | agccagcgtc | ggcggcgcga | atggcgtggc |
|------|------------|------------|------------|------------|------------|------------|
| 120  | gttctcggcc | ctctcgagtg | cggggccggg | gcccggggcc | ccctgtgcgt | ctcgccctgg |
| 180  | cgtctcggag | cggtgtggag | accaacctga | ggacccgcag | tcgagtacgt | gtggtaaaca |
| 240  | gggcgtcccg | atggcctggt | gagggcgcgc | ctcgcccaag | tcggcgacag | agtggccgct |
| 300  | cgtgcccgag | cgcgcttctt | gcgcccgaca | cgagggctgc | gcggagacct | tgggcgcccg |
| 360  | ctgcaccttc | ctcgtggggg | gccctggtgg | gccctgggtc | gaggggccgc | cccggcggcc |
| 420  | ctacaatgag | ccgtcgtcct | aacgcctcgg | ggcgcggagg | tgctggtggc | aaggacaagg |
| 480  | tatagtggtc | gaacaggaaa | tctcacgcgg | cttgcccatg | ggaacatcac | gagcgctacg |
| 540  | aggaattcca | tggtgcaaaa | attttggagc | aggaagagaa | gctatccaaa | attatgatta |
| 600  | cggtcagtct | agttcatcag | catgtacagg | tggcacccgg | ccataggggt | gtaacgatga |
| 660  | ctggctaata | tctcgttagc | atgatgatta | cttcatcacc | tggccattgc | gtggtgtttg |
| 720  | gagccataga | ttggaagtca | ggctctcaga | cctatatact | tacagcgttt | ttttactata |
| 780  | tggagaaaag | ctgtaaagca | ctacttcata | tggccagctt | agaaagttat | aaagaaacta |
| 840  | agtaaaggat | aaaatttcaa | gtgtgtattg | aaattgtgca | ttgatgctga | ggaattgatg |
| 900  | cccatggctt | tatgcattga | tttcatagaa | caagcatatt | ttctgccatg | attattagaa |
| 960  | aggatattgg | tcaaagccct | cttgatgtca | aatgtgtaaa | gaacatgtcc | ttggatcacc |
| 1020 | aagggatcca | ctcctcctgg | gctccagaat | ggagatgcct | gggatgtaca | ggagagcctg |
| 1080 | cagtccacca | gtgatgagag | gatgacggaa | tttaccagat | tgagtctagc | gctgcaaatt |
| 1140 | agatgcagga | gctttaaagg | tgtgatccca | tgagccacag | ctgctgaatc | tcagcctccc |
| 1200 | acccatctcc | ggcatggagg | agtgactctc | agccggcagg | cattgctaga | gaaaatacgg |

⟨210⟩ 109

<211> 576

<212> DNA

<213> Homo sapiens

<400> 109

| g 60  | cttgggcctg | tggattattc | ccagtgttac | catcctgctg | cactgaaact | atgttttgcc |
|-------|------------|------------|------------|------------|------------|------------|
| g 120 | agctctgatg | tgggtgattc | acagtccatg | gcctgagcta | atgtttcccc | aatgacttga |
| a 180 | gactctgtca | agatagactg | tgtatattca | agaagacaaa | tccagagcac | ggatgtgttt |
| t 240 | cagtgtgcct | actccaatct | ctatactatt | cgaatatgtg | acgccaagga | ccaggagagc |
| t 300 | tgatggctct | acttatgcaa | atgggggaca | cgtacacttg | tccagaaccg | attgggcgct |
| c 360 | aatccgcctc | atatctgtga | cagggaacct | agaggctgac | aagatgtgca | ctcctgctcc |
| c 420 | agaggagccc | atgtgcttcc | gtggtactgc | caagaaggcg | gccaggtgtt | aaaggggaga |
| a 480 | ccagagcaca | gatgtgtttt | attcagatgg | gggtggattg | tggtccatgt | aaagagctca |
| a 540 | aaaggtaaca | gacggcgcgc | atattttcag | ggtagaatgg | acgtgaccaa | gaagtgaaac |
| 576   |            |            | tctggc     | tagagaaggc | atcactgtgt | aggaggaaac |

<210> 110

<211> 780

<212> DNA

<213> Homo sapiens

<400> 110

60 atggcggggt cgccgctgct ctgggggccg cgggccgggg gcgtcggcct tttggtgctg 120 ctgctgctcg gcctgtttcg gccgccccc gcgctctgcg cgcggccggt aaaggagccc cgcggcctaa gcgcagcgtc tccgcccttg gctgagactg gcgctcctcg ccgcttccgg 180 240 cggtcagtgc cccgaggtga ggcggcgggg gcggtgcagg agctggcgcg ggcgctggcg 300 catcigcing aggccgaacg traggagrag graceggragg aggraggaggat graceggraggat 360 cagcaggege gegteetgge geagetgetg egegtetggg gegeeeceeg caactetgat 420 ceggetetgg geetggacga egaceeegac gegeetgeag egeagetege tegegetetg 480 ctecgegece geettgacee tgeegeete géageceage ttgteceege geeegteece

| gccgcg  | gcgc  | tccg | accc | cg g | cccc | cggt | c ta | cgac | gacg | gcc | ccgc | ggg | cccg | gatgc  | t 540 |
|---|-------|------|------|------|------|------|------|------|------|-----|------|-----|------|--------|-------|
| gaggag  | gcag  | gcga | cgag | ac a | cccg | acgt | g ga | cccc | gagc | tgt | tgag | gta | cttg | ctggg  | a 600 |
| cggatt  | cttg  | cggg | aagc | gc g | gact | ccga | g gg | ggtg | gcag | ссс | cgcg | ccg | cctc | cgccg  | t 660 |
| gccgcc  | gacc  | acga | tgtg | gg c | tctg | agct | g cc | ccct | gagg | gcg | tgct | ggg | ggcg | ctgct  | g 720 |
| cgtgtg  | aaac  | gcct | agag | ac c | ccgg | cgcc | с са | ggtg | cctg | cac | gccg | cct | cttg | ccacco | c 780 |
|   |       |      |      |      |      |      |      |      |      |     |      |     |      |        |       |
| <210>   | 111   |      |      |      |      |      |      |      |      |     |      |     |      | ٠      |       |
| <211>   | 1633  |      |      |      |      |      |      |      |      |     |      |     |      |        |       |
| <212>   | DNA   |      |      |      |      |      |      |      |      |     |      |     |      |        |       |
| <213>   | Homo  | sapi | ens  |      |      |      |      |      |      |     |      |     |      |        |       |
| <220>   |       |      |      |      |      |      |      |      |      |     |      |     |      |        |       |
| <221>   | CDS   |      |      |      |      |      |      |      |      |     |      |     |      |        |       |
| <222>   | (68). | (1   | 498) |      |      |      |      |      |      |     |      |     |      |        |       |
| <400>   | 111   |      |      |      |      |      |      |      |      |     |      |     |      |        |       |
| acaaccggct ggggtccttg cgcgccgcgg ctcagggagg agcaccgact gcgccgcacc |       |      |      |      |      |      |      | 60   |      |     |      |     |      |        |       |
| ctgaga  | g atg | gtt  | ggt  | gcc  | atg  | tgg  | aag  | gtg  | att  | gtt | tcg  | ctg | gtc  | ctg    | 109   |
|   | Met   | Val  | G1 y | Ala  | Met  | Trp  | Lys  | Val  | Ile  | Val | Ser  | Leu | Val  | Leu    |       |
|   | 1     |      |      |      | 5    |      |      |      |      | 10  |      |     |      |        |       |
| ttg at  | g cct | ggc  | ccc  | tgt  | gat  | ggg  | ctg  | ttt  | cgc  | tcc | cta  | tac | aga  | agt    | 157   |
| Leu Me  | t Pro | Gly  | Pro  | Cys  | Asp  | Gly  | Leu  | Phe  | Arg  | Ser | Leu  | Tyr | Arg  | Ser    |       |
| 15  |       |      |      | 20   |      |      |      |      | 25   |     |      |     |      | 30     |       |
| gtt tc  | c atg | cca  | cct  | aag  | gga  | gac  | tca  | gga  | cag  | cca | tta  | ttt | ctc  | acc    | 205   |
| Val Se  | r Met | Pro  | Pro  | Lys  | Gly  | Asp  | Ser  | Gly  | Gln  | Pro | Leu  | Phe | Leu  | Thr    |       |
|   |       |      | 35   |      |      |      |      | 40   | ٠.   |     |      |     | 45   |        |       |
| cct ta  | c att | gaa  | gct  | ggg  | aag  | atc  | caa  | aaa  | gga  | aga | gaa  | ttg | agt  | ttg    | 253   |

| Pro | Tyr | He  | Glu | Ala | Gly | Lys | He  | Gln | Lys | Gly | Arg | Glu | Leu | Ser | Leu |     |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
|     |     |     | 50  |     |     |     |     | 55  |     |     |     |     | 60  |     |     |     |
| gtc | ggc | cct | ttc | cca | gga | ctg | aac | atg | aag | agt | tat | gcc | ggc | ttc | ctc | 301 |
| Val | Gly | Pro | Phe | Pro | Gly | Leu | Asn | Met | Lys | Ser | Tyr | Ala | Gly | Phe | Leu |     |
|     |     | 65  |     |     |     |     | 70  |     |     |     |     | 75  |     |     |     |     |
| acc | gtg | aat | aag | act | tac | aac | agc | aac | ctc | ttc | ttc | tgg | ttc | ttc | cca | 349 |
| Thr | Val | Asn | Lys | Thr | Tyr | Asn | Ser | Asn | Leu | Phe | Phe | Trp | Phe | Phe | Pro |     |
|     | 80  |     |     |     |     | 85  |     |     |     |     | 90  |     |     |     |     |     |
| gct | cag | ata | cag | cca | gaa | gat | gcc | cca | gta | gtt | ctc | tgg | cta | cag | ggt | 397 |
| Ala | Gln | Ile | Gln | Pro | Glu | Asp | Ala | Pro | Val | Val | Leu | Trp | Leu | Gln | Gly |     |
| 95  |     |     |     |     | 100 |     |     |     |     | 105 |     |     |     |     | 110 |     |
| ggg | ccg | gga | ggt | tca | tcc | atg | ttt | gga | ctc | ttt | gtg | gaa | cat | ggg | cct | 445 |
| Gly | Pro | Gly | Gly | Ser | Ser | Met | Phe | Gly | Leu | Phe | Val | Glu | His | Gly | Pro |     |
|     |     |     |     | 115 |     |     |     |     | 120 |     |     |     |     | 125 |     |     |
| tat | gtt | gtc | aca | agt | aac | atg | acc | ttg | cgt | gac | aga | gac | ttc | ccc | tgg | 493 |
| Tyr | Val | Val | Thr | Ser | Asn | Met | Thr | Leu | Arg | Asp | Arg | Asp | Phe | Pro | Trp |     |
|     |     |     | 130 |     |     |     |     | 135 |     |     |     |     | 140 |     |     |     |
| acc | aca | acg | ctc | tcc | atg | ctt | tac | att | gac | aat | cca | gtg | ggc | aca | ggc | 541 |
| Thr | Thr | Thr | Leu | Ser | Met | Leu | Tyr | Ile | Asp | Asn | Pro | Val | Gly | Thr | Gly |     |
|     |     | 145 |     |     |     |     | 150 |     |     |     |     | 155 |     |     |     |     |
| ttc | agt | ttt | act | gat | gat | acc | cac | gga | tat | gca | gtc | aat | gag | gac | gat | 589 |
| Phe | Ser | Phe | Thr | Asp | Asp | Thr | His | Gly | Tyr | Ala | Val | Asn | Glu | Asp | Asp |     |
|     | 160 |     |     |     |     | 165 |     |     |     |     | 170 |     |     |     |     |     |
| gta | gca | cgg | gat | tta | tac | agt | gca | cta | att | cag | ttt | ttc | cag | ata | ttt | 637 |
| Val | Ala | Arg | Asp | Leu | Tyr | Ser | Ala | Leú | Ile | Gln | Phe | Phe | Gln | He  | Phe |     |

| 175  |     |     |     |      | 180 |     |     |     |     | 185 |     |     |     |     | 190 |      |
|------|-----|-----|-----|------|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|------|
| cct  | gaa | tat | aaa | aat. | aat | gac | ttt | tat | gtc | act | ggg | gag | tct | tat | gca | 685  |
| Pro  | Glu | Tyr | Lys | Asn  | Asn | Asp | Phe | Tyr | Val | Thr | Gly | Glu | Ser | Tyr | Ala |      |
|      |     |     |     | 195  |     |     |     |     | 200 |     |     |     |     | 205 |     |      |
| ggg  | aaa | tat | gtg | cca  | gcc | att | gca | cac | ctc | atc | cat | tcc | ctc | aac | cct | 733  |
| G1 y | Lys | Tyr | Val | Pro  | Ala | Ile | Ala | His | Leu | Ile | His | Ser | Leu | Asn | Pro |      |
|      |     |     | 210 |      |     |     |     | 215 | ٠   |     |     |     | 220 |     |     |      |
| gtg  | aga | gag | gtg | aag  | atc | aac | ctg | aac | gga | att | gct | att | gga | gat | gga | 781  |
| Val  | Arg | Glu | Val | Lys  | Ile | Asn | Leu | Asn | Gly | Ile | Ala | Ile | Gly | Asp | Gly |      |
|      |     | 225 |     |      |     |     | 230 |     |     |     |     | 235 |     |     |     |      |
| tat  | tct | gat | ccc | gaa  | tca | att | ata | ggg | ggc | tat | gca | gaa | ttc | ctg | tac | 829  |
| Tyr  | Ser | Asp | Pro | Glu  | Ser | Ile | Ile | Gly | Gly | Tyr | Ala | Glu | Phe | Leu | Tyr |      |
|      | 240 |     |     |      |     | 245 |     |     |     |     | 250 |     |     |     |     |      |
| caa  | att | ggc | ttg | ttg  | gat | gag | aag | caa | aaa | aag | tac | ttc | cag | aag | cag | 877  |
| Gln  | He  | Gly | Leu | Leu  | Asp | Glu | Lys | Gln | Lys | Lys | Tyr | Phe | Gln | Lys | Gln |      |
| 255  |     |     |     |      | 260 |     |     |     |     | 265 |     |     |     |     | 270 |      |
| tgc  | cat | gaa | tgc | ata  | gaa | cac | atc | agg | aag | cag | aac | tgg | ttt | gag | gcc | 925  |
| Cys  | His | Glu | Cys | Ile  | Glu | His | Ile | Arg | Lys | Gln | Asn | Trp | Phe | Glu | Ala |      |
|      |     |     |     | 275  |     | ,   |     |     | 280 |     |     |     |     | 285 |     |      |
| ttt  | gaa | ata | ctg | gat  | aaa | cta | cta | gat | ggc | gac | tta | aca | agt | gat | cct | 973  |
| Phe  | Glu | Ile | Leu | Asp  | Lys | Leu | Leu | Asp | Gly | Asp | Leu | Thr | Ser | Asp | Pro |      |
|      |     |     | 290 |      |     |     |     | 295 |     |     |     |     | 300 |     |     |      |
| tct  | tac | ttc | cag | aat  | gtt | aca | gga | tgt | agt | aat | tac | tat | aac | ttt | ttg | 1021 |
| Ser  | Tyr | Phe | Gln | Asn  | Val | Thr | Gly | Cys | Ser | Asn | Tyr | Tyr | Asn | Phe | Leu |      |
|      |     | 305 |     |      |     |     | 310 |     |     |     |     | 315 |     |     |     |      |

| cgg | tgc | acg | gaa              | cct | gag | gat | cag | ctt | tac        | tat | gtg | aaa | ttt | ttg | tca | 1069 |
|-----|-----|-----|------------------|-----|-----|-----|-----|-----|------------|-----|-----|-----|-----|-----|-----|------|
| Arg | Cys | Thr | Glu <sub>.</sub> | Pro | Glu | Asp | Gln | Leu | Tyr        | Tyr | Val | Lys | Phe | Leu | Ser |      |
|     | 320 |     |                  |     |     | 325 |     |     |            |     | 330 |     |     |     |     |      |
| ctc | cca | gag | gtg              | aga | caa | gcc | atc | cac | gtg        | ggg | aat | cag | act | ttt | aat | 1117 |
| Leu | Pro | Glu | Val              | Arg | Gln | Ala | Ile | His | Val        | Gly | Asn | Gln | Thr | Phe | Asn |      |
| 335 |     |     |                  |     | 340 |     |     |     |            | 345 |     |     |     |     | 350 |      |
| gat | gga | act | ata              | gtt | gaa | aag | tac | ttg | cga        | gaa | gat | aca | gta | cag | tca | 1165 |
| Asp | Gly | Thr | Ile              | Val | Glu | Lys | Tyr | Leu | Arg        | Glu | Asp | Thr | Val | Gln | Ser |      |
|     |     |     |                  | 355 |     |     |     |     | 360        |     |     |     |     | 365 |     |      |
| gtt | aag | cca | tgg              | tta | act | gaa | atc | atg | aat        | aat | tat | aag | gtt | ctg | atc | 1213 |
| Val | Lys | Pro | Trp              | Leu | Thr | Glu | Ile | Met | Asn        | Asn | Tyr | Lys | Val | Leu | He  |      |
|     |     |     | 370              |     |     |     |     | 375 |            |     |     |     | 380 |     |     |      |
| tac | aat | ggc | caa              | ctg | gac | atc | atc | gtg | gca        | gct | gcc | ctg | aca | gag | cac | 1261 |
| Tyr | Asn | Gly | Gln              | Leu | Asp | Ile | Ile | Val | Ala        | Ala | Ala | Leu | Thr | Glu | His |      |
|     |     | 385 |                  |     |     |     | 390 |     |            |     |     | 395 |     |     |     |      |
| tcc | ttg | atg | ggc              | atg | gac | tgg | aaa | gga | tcc        | cag | gaa | tac | aag | aag | gca | 1309 |
| Ser | Leu | Met | Gly              | Met | Asp | Trp | Lys | Gly | Ser        | Gln | Glu | Tyr | Lys | Lys | Ala |      |
|     | 400 |     |                  |     |     | 405 |     |     |            |     | 410 |     |     |     |     |      |
| gaa | aaa | aaa | gtt              | tgg | aag | atc | ttt | aaa | tct        | gac | agt | gaa | gtg | gct | ggt | 1357 |
| Glu | Lys | Lys | Val              | Trp | Lys | Ile | Phe | Lys | Ser        | Asp | Ser | Glu | Val | Ala | Gly |      |
| 415 |     |     |                  |     | 420 |     |     |     |            | 425 |     |     |     |     | 430 |      |
| tac | atc | cgg | caa              | gcg | ggt | gac | ttc | cat | cag        | gta | att | att | cga | ggt | gga | 1405 |
| Tyr | Ile | Arg | Gln              | Ala | Gly | Asp | Phe | His | Gln        | Val | Ile | Ile | Arg | Gly | Gly |      |
|     |     |     |                  | 435 |     |     |     |     | 440        |     |     |     |     | 445 |     |      |
| gga | cat | att | tta              | ссс | tat | gac | cag | cct | نىر<br>ctg | aga | gct | ttt | gac | atg | att | 1453 |
|     |     |     |                  |     |     |     |     |     |            |     |     |     |     |     |     |      |

| Gly His Il  | e Leu Pro | Tyr Asp   | Gln Pro           | Leu Arg  | Ala Phe  | Asp Met Ile    |      |
|-------------|-----------|-----------|-------------------|----------|----------|----------------|------|
|             | 450       |           | 455               |          |          | 460            |      |
| aat cga tt  | c att tat | gga aaa   | gga tgg           | gat cct  | tat gtt  | gga taaac      | 1500 |
| Asn Arg Ph  | e Ile Tyr | Gly Lys   | Gly Trp           | Asp Pro  | Tyr Val  | Gly            |      |
| 46          | 5         |           | 470               |          | 475      |                |      |
| taccttccca  | aaagagaa  | ca tcagag | gttt tca          | attgctga | aaagaaaa | atc gtaaaaacag | 1560 |
| aaaatgtcat  | aggaataa  | aa aaatta | tctt ttc          | catatotg | caagatti | tt ttcatcaata  | 1620 |
| aaaattatcc  | ttg       |           |                   |          |          |                | 1633 |
|             |           |           |                   |          |          |                |      |
| <210> 112   |           |           |                   |          |          |                |      |
| <211> 1095  |           |           |                   |          |          |                | ٠    |
| <212> DNA   |           |           |                   |          |          |                |      |
| <213> Homo  | sapiens   | •         |                   |          |          |                |      |
| <220>       |           |           |                   |          |          |                |      |
| <221> CDS   |           |           |                   |          |          |                |      |
| <222> (192) | ) (872)   |           |                   |          |          |                |      |
| <400> 112   |           |           |                   |          |          |                |      |
| ctttaaaatg  | tcattggta | a accata  | c <b>ttg a</b> tc | ctaaatt  | cctgtact | tc ctcaggccat  | 60   |
| ccgagcatga  | aacgctgto | a cctacco | caca tcc          | gctggct  | gtgacgct | tg tcaaagtgtt  | 120  |
| ctctatcggc  | tgcatgcct | a gaccaco | caaa gcg          | ttctgac  | cggacagt | gt cactggagaa  | 180  |
| ggcggcgcga  | c atg tco | agg gcg   | cag atc           | tgg gct  | ctg gtg  | tct ggt gtc    | 230  |
|             | Met Ser   | Arg Ala   | Gln Ile           | Trp Ala  | Leu Val  | Ser Gly Val    |      |
|             | 1         |           | 5                 |          | 10       |                |      |
| gga ggg tti | t gga gct | ctc gtt g | gct gct           | acc_acg  | tcc aat  | gag tgg aaa    | 278  |

Gly Gly Phe Gly Ala Leu Val Ala Ala Thr Thr Ser Asn Glu Trp Lys

|     | 15  |     |     |     |     | 20  |     |     |           |     | 25  |     |     |     |     |     |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----------|-----|-----|-----|-----|-----|-----|-----|
| gtg | acc | acg | cga | gcc | tcc | tcg | gtg | ata | aca       | gcc | ạct | tgg | gtt | tac | cag | 326 |
| Val | Thr | Thr | Arg | Ala | Ser | Ser | Val | Ile | Thr       | Ala | Thr | Trp | Val | Tyr | Gln |     |
| 30  |     |     |     |     | 35  |     |     |     |           | 40  |     |     |     |     | 45  |     |
| ggt | ctg | tgg | atg | aac | tgc | gca | ggt | aac | gcg       | ttg | ggt | tct | ttc | cat | tgc | 374 |
| Gly | Leu | Trp | Met | Asn | Cys | Ala | Gly | Asn | Ala       | Leu | Gly | Ser | Phe | His | Cys |     |
|     |     |     |     | 50  |     |     |     |     | 55        |     |     |     |     | 60  |     |     |
| cga | ccg | cat | ttt | act | atc | ttc | aaa | gta | gca       | ggt | tat | ata | cag | gca | tgt | 422 |
| Arg | Pro | His | Phe | Thr | He  | Phe | Lys | Val | Ala       | Gly | Tyr | Ile | Gln | Ala | Cys |     |
|     |     |     | 65  |     |     |     |     | 70  |           |     |     |     | 75  |     |     |     |
| aga | gga | ctt | atg | atc | gct | gct | gtc | agc | ctg       | ggc | ttc | ttt | ggt | tcc | ata | 470 |
| Arg | Gly | Leu | Met | lle | Ala | Ala | Val | Ser | Leu       | Gly | Phe | Phe | Gly | Ser | Ile |     |
|     |     | 80  |     |     |     |     | 85  |     |           |     |     | 90  |     |     |     |     |
| ttt | gcg | ctc | ttt | gga | atg | aag | tgt | acc | aaa       | gtc | gga | ggc | tcc | gat | aaa | 518 |
| Phe | Ala | Leu | Phe | Gly | Met | Lys | Cys | Thr | Lys       | Val | Gly | Gly | Ser | Asp | Lys |     |
|     | 95  |     |     |     |     | 100 |     |     |           |     | 105 |     |     |     |     |     |
| gcc | aaa | gct | aaa | att | gct | tgt | ttg | gct | ggg       | att | gta | ttc | ata | ctg | tca | 566 |
| Ala | Lys | Ala | Lys | Ile | Ala | Cys | Leu | Ala | Gly       | Ile | Val | Phe | Ile | Leu | Ser |     |
| 110 |     |     |     |     | 115 |     |     |     |           | 120 |     |     |     |     | 125 |     |
|     |     |     |     |     | act |     |     |     |           |     |     |     |     |     |     | 614 |
| Gly | Leu | Cys | Ser |     | Thr | Gly | Cys | Ser |           | Tyr | Ala | Asn | Lys |     | Thr |     |
|     |     |     |     | 130 |     |     |     |     | 135       |     |     |     |     | 140 |     |     |
|     |     |     |     |     | cct |     |     |     |           |     |     |     |     |     |     | 662 |
| Thr | Glu | Phe |     | Asp | Pro | Leu | Phe |     | Glu<br>ښر | Gln | Lys | Tyr |     | Leu | Gly |     |
|     |     |     | 145 |     |     |     |     | 150 |           |     |     |     | 155 |     |     |     |

| gcc  | gct  | ctg   | ttt  | att  | gga  | tgg  | gca  | gga | gcc  | tca | ctg  | tgc   | ata   | att  | ggt   | 710  |
|------|------|-------|------|------|------|------|------|-----|------|-----|------|-------|-------|------|-------|------|
| Ala  | Ala  | Leu   | Phe  | Ile  | Gly  | Trp  | Ala  | Gly | Ąla  | Ser | Leu  | Cys   | Ile   | Ile  | Gly   |      |
|      |      | 160   |      |      |      |      | 165  |     |      |     |      | 170   |       |      |       |      |
| ggt  | gtc  | ata   | ttt  | tgc  | ttt  | tca  | ata  | tct | gac  | aac | aac  | aaa   | aca   | ссс  | aga   | 758  |
| Gly  | Val  | Ile   | Phe  | Cys  | Phe  | Ser  | Ile  | Ser | Asp  | Asn | Asn  | Lys   | Thr   | Pro  | Arg   |      |
|      | 175  |       |      |      |      | 180  |      |     |      |     | 185  |       |       |      |       |      |
| tac  | aca  | tac   | aac  | ggg  | gcc  | aca  | tct  | gtc | atg  | tct | tct  | cgg   | aca   | aag  | tat   | 806  |
| Tyr  | Thr  | Tyr   | Asn  | Gly  | Ala  | Thr  | Ser  | Val | Met  | Ser | Ser  | Arg   | Thr   | Lys  | Tyr   |      |
| 190  |      |       |      |      | 195  |      |      |     |      | 200 |      |       |       |      | 205   |      |
| cat  | ggt  | gga   | gaa  | gat  | ttt  | aaa  | aca  | aca | aac  | cct | tca  | aaa   | cag   | ttt  | gat   | 854  |
| His  | Gly  | Gly   | Glu  | Asp  | Phe  | Lys  | Thr  | Thr | Asn  | Pro | Ser  | Lys   | Gln   | Phe  | Asp   |      |
|      |      |       |      | 210  |      |      |      |     | 215  |     | •    |       |       | 220  |       |      |
| aaa  | aat  | gct   | tat  | gtc  | t aa | aaga | gcto | gcg | ggca | agc | tgcc | etett | ga    |      |       | 900  |
| Lys  | Asn  | Ala   | Tyr  | Val  |      |      |      |     |      |     |      |       |       |      |       |      |
|      |      |       | 225  |      |      |      |      |     |      |     |      |       |       |      |       |      |
| gttt | gtta | ıta a | aagc | gaac | t gt | tcac | aaaa | tga | tccc | atc | aagg | ccct  | cc c  | ataa | ttaac | 960  |
| actc | aaaa | ict a | ittt | taaa | a ta | tgca | tttg | aag | cato | tgt | tgat | tgta  | ıtg g | atgt | aagtg | 1020 |
|      |      |       |      |      |      |      |      |     |      |     |      |       |       |      | ataaa | 1080 |
| cagt |      |       |      |      |      |      |      |     |      |     |      |       |       |      |       | 1095 |

<210> 113

<211> 1602

<212> DNA

<213> Homo sapiens

<220>

| <221 | > CI  | )S    |       |       |       |       |       |       |           |       |       |       |       |       |       |     |
|------|-------|-------|-------|-------|-------|-------|-------|-------|-----------|-------|-------|-------|-------|-------|-------|-----|
| <222 | ?> (3 | 34)   | . (95 | 51)   |       |       |       |       |           |       |       |       |       |       |       |     |
| <400 | )> 11 | 3     |       |       |       |       |       |       |           |       |       |       |       |       |       |     |
| ttte | gtcag | ggt g | ggtgg | gagga | na aa | iggce | gctco | e gto | e ate     | g ggg | gato  | c ca  | g ac  | g ago | ccc   | 54  |
|      |       |       |       |       |       |       |       |       | Met       | t Gly | / I1e | e Gli | ı Thi | r Sei | r Pro |     |
|      |       |       |       |       |       |       |       |       | 1         | l     |       |       |       | 5     |       |     |
| gtc  | ctg   | ctg   | gcc   | tcc   | ctg   | ggg   | gtg   | ggg   | ctg       | gtc   | act   | ctg   | ctc   | ggc   | ctg   | 102 |
| Val  | Leu   | Leu   | Ala   | Ser   | Leu   | Gly   | Val   | Gly   | Leu       | Val   | Thr   | Leu   | Leu   | Gly   | Leu   |     |
|      |       | 10    |       |       |       |       | 15    |       |           |       |       | 20    |       |       |       |     |
| gct  | gtg   | ggc   | tcc   | tac   | ttg   | gtt   | cgg   | agg   | tcc       | cgc   | cgg   | cct   | cag   | gtc   | act   | 150 |
| Ala  | Val   | Gly   | Ser   | Tyr   | Leu   | Val   | Arg   | Arg   | Ser       | Arg   | Arg   | Pro   | Gln   | Val   | Thr   |     |
|      | 25    |       |       |       |       | 30    |       |       |           |       | 35    |       | ٠     |       |       |     |
| ctc  | ctg   | gac   | ccc   | aat   | gaa   | aag   | tac   | ctg   | cta       | cga   | ctg   | cta   | gac   | aag   | acg   | 198 |
| Leu  | Leu   | Asp   | Pro   | Asn   | Glu   | Lys   | Tyr   | Leu   | Leu       | Arg   | Leu   | Leu   | Asp   | Lys   | Thr   |     |
| 40   |       |       |       |       | 45    |       |       |       |           | 50    |       |       |       |       | 55    |     |
| act  | gtg   | agc   | cac   | aac   | acc   | aag   | agg   | ttc   | cgc       | ttt   | gcc   | ctg   | ссс   | acc   | gcc   | 246 |
| Thr  | Val   | Ser   | His   | Asn   | Thr   | Lys   | Arg   | Phe   | Arg       | Phe   | Ala   | Leu   | Pro   | Thr   | Λla   |     |
|      |       |       |       | 60    |       |       |       |       | 65        |       |       |       |       | 70    |       |     |
| cac  | cac   | act   | ctg   | ggg   | ctg   | cct   | gtg   | ggc   | aaa       | cat   | atc   | tac   | ctc   | tcc   | acc   | 294 |
| His  | His   | Thr   | Leu   | Gly   | Leu   | Pro   | Val   | Gly   | Lys       | His   | Ile   | Tyr   | Leu   | Ser   | Thr   |     |
|      |       |       | 75    |       |       |       |       | 80    |           |       |       |       | 85    |       |       |     |
| cga  | att   | gat   | ggc   | agc   | ctg   | gtc   | atc   | agg   | cca       | tac   | act   | cct   | gtc   | acc   | agt   | 342 |
| Arg  | Ile   | Asp   | Gly   | Ser   | Leu   | Val   | Ile   | Arg   | Pro       | Tyr   | Thr   | Pro   | Val   | Thr   | Ser   |     |
|      |       | 90    |       |       |       |       | 95    |       |           |       |       | 100   |       |       |       |     |
| gat  | gag   | gat   | caa   | ggc   | tat   | gtg   | gat   | ctt   | نر<br>gtc | atc   | aag   | gtc   | tac   | ctg   | aag   | 390 |

| Asp | Glu | Asp | Gln | Gly | Tyr | Val | Asp | Leu | Val       | Ile | Lys | Val | Tyr | Leu | Lys |     |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----------|-----|-----|-----|-----|-----|-----|-----|
|     | 105 |     |     |     |     | 110 |     |     |           |     | 115 |     |     |     |     |     |
| ggt | gtg | cac | ссс | aaa | ttt | cct | gag | gga | ggg       | aag | atg | tct | cag | tac | ctg | 438 |
| Gly | Val | His | Pro | Lys | Phe | Pro | Glu | Gly | Gly       | Lys | Met | Ser | G1n | Tyr | Leu |     |
| 120 |     |     |     |     | 125 |     |     |     |           | 130 |     |     |     |     | 135 |     |
| gat | agc | ctg | aag | gtt | ggg | gat | gtg | gtg | gag       | ttt | cgg | ggg | cca | agc | ggg | 486 |
| Asp | Ser | Leu | Lys | Val | Gly | Asp | Val | Val | Glu       | Phe | Arg | Gly | Pro | Ser | Gly |     |
|     |     |     |     | 140 |     |     |     |     | 145       |     |     |     |     | 150 |     |     |
| ttg | ctc | act | tac | act | gga | aaa | ggg | cat | ttt       | aac | att | cag | ccc | aac | aag | 534 |
| Leu | Leu | Thr | Tyr | Thr | Gly | Lys | Gly | His | Phe       | Asn | Ile | Gln | Pro | Asn | Lys |     |
|     |     |     | 155 |     |     |     |     | 160 |           |     |     |     | 165 |     |     |     |
| aaa | tct | cca | cca | gaa | ccc | cga | gtg | gcg | aag       | aaa | ctg | gga | atg | att | gcc | 582 |
| Lys | Ser | Pro | Pro | Glu | Pro | Arg | Val | Ala | Lys       | Lys | Leu | Gly | Met | Ile | Ala |     |
|     |     | 170 |     |     |     |     | 175 |     |           |     |     | 180 |     |     |     |     |
| ggc | ggg | aca | gga | atc | acc | cca | atg | cta | cag       | ctg | atc | cgg | gcc | atc | ctg | 630 |
| Gly | Gly | Thr | Gly | Ile | Thr | Pro | Met | Leu | Gln       | Leu | Ile | Arg | Ala | Ile | Leu |     |
|     | 185 |     |     |     |     | 190 |     |     |           |     | 195 |     |     |     |     |     |
| aaa | gtc | cct | gaa | gat | cca | acc | cag | tgc | ttt       | ctg | ctt | ttt | gcc | aac | cag | 678 |
| Lys | Val | Pro | Glu | Asp | Pro | Thr | Gln | Cys | Phe       | Leu | Leu | Phe | Ala | Asn | Gln |     |
| 200 |     |     |     |     | 205 | •   |     |     |           | 210 |     |     |     |     | 215 |     |
| aca | gaa | aag | gat | atc | atc | ttg | cgg | gag | gac       | tta | gag | gaa | ctg | cag | gcc | 726 |
| Thr | Glu | Lys | Asp | Ile | Ile | Leu | Arg | Glu | Asp       | Leu | Glu | Glu | Leu | Gln | Ala |     |
|     |     |     |     | 220 |     |     |     |     | 225       |     |     |     |     | 230 |     |     |
| cgc | tat | ccc | aat | cgc | ttt | aag | ctc | tgg | ttc<br>سر | act | ctg | gat | cat | ccc | cca | 774 |
| Arg | Tvr | Pro | Asn | Arg | Phe | Lvs | Leu | Trn | Phe       | Thr | Lau | Acn | ніс | Dro | Dwa |     |

|        |        | 235   |       |       |      |       | 240   |      |      |      |      | 245  |      |        |      |
|--------|--------|-------|-------|-------|------|-------|-------|------|------|------|------|------|------|--------|------|
| aaa ga | at tgg | gcc   | tac   | agc   | aag  | ggc   | ttt   | gtg  | act  | gcc  | gac  | atg  | atc  | cgg    | 822  |
| Lys As | sp Trp | Ala   | Tyr   | Ser   | Lys  | Gly   | Phe   | Val  | Thr  | Ala  | Asp  | Met  | Ile  | Arg    |      |
|        | 250    |       |       |       |      | 255   |       |      |      |      | 260  |      |      |        |      |
| gaa ca | ac ctg | ccc   | gct   | cca   | ggg  | gat   | gat   | gtg  | ctg  | gta  | ctg  | ctt  | tgt  | ggg    | 870  |
| Glu Hi | is Leu | Pro   | Ala   | Pro   | Gly  | Asp   | Asp   | Val  | Leu  | Val  | Leu  | Leu  | Cys  | Gly    |      |
| 26     | 65     |       |       |       | 270  |       |       |      |      | 275  |      |      |      |        |      |
| cca co | сс сса | atg   | gtg   | cag   | ctg  | gcc   | tgc   | cat  | ccc  | aac  | ttg  | gac  | aaa  | ctg    | 918  |
| Pro Pr | ro Pro | Met   | Val   | Gln   | Leu  | Ala   | Cys   | His  | Pro  | Asn  | Leu  | Asp  | Lys  | Leu    |      |
| 280    |        |       |       | 285   |      |       |       |      | 290  |      |      |      |      | 295    |      |
| ggc ta | ac tca | caa   | aag   | atg   | cga  | ttc   | acc   | tac  | tg a | agca | tcct | cc a | gctt | ccctg  | 970  |
| Gly Ty | yr Ser | Gln   | Lys   | Met   | Arg  | Phe   | Thr   | Tyr  |      |      |      |      |      |        |      |
|        |        |       | 300   |       |      |       |       | 305  |      |      |      |      |      |        |      |
| gtgctg | gttcg  | ctgca | gttg  | gt to | ccc  | atca  | g ta  | ctca | agca | cta  | taag | cct  | taga | ttcctt | 1030 |
| tcctca | agagt  | ttcag | gttt  | t ti  | tcag | ttaca | a tc  | taga | gctg | aaa  | tetg | gat  | agta | cctgca | 1090 |
| ggaaca | aatat  | tcctg | gtago | c at  | tgga | agagı | g gc  | caag | gctc | agto | cact | cct  | tgga | tggcct | 1150 |
| cctaaa | atctc  | cccgt | ggca  | ia ca | aggt | ccag  | g aga | aggc | ccat | gga  | gcag | tct  | cttc | catgga | 1210 |
| gtaaga | aagga  | aggga | ıgcat | g ta  | acgc | ttgg  | t cc  | aaga | ttgg | cta  | gttc | ctt  | gata | gcatct | 1270 |
| tactc  | tcacc  | ttctt | tgtg  | gt ci | tgtg | atga  | a ag  | gaac | agtc | tgt  | gcaa | tgg  | gttt | tactta | 1330 |
| aactt  | cactg  | ttcaa | ccta  | it ga | agca | aatc  | t gt  | atgt | gtga | gta  | taag | ttg  | agca | tagcat | 1390 |
| actte  | cagag  | gtggt | ctta  | it g  | gaga | tggc  | a ag  | aaag | gagg | aaa  | tgat | ttc  | ttca | gatete | 1450 |
| aaagg  | agtct  | gaaat | tatca | it a  | tttc | tgtg  | t gt  | gtct | ctct | cag  | cccc | tgc  | ccag | gctaga | 1510 |
| gggaa  | acagc  | tactg | gataa | at c  | gaaa | actg  | c tg  | tttg | tggc | agg  | aacc | cct  | ggct | gtgcaa | 1570 |
| ataaa  | tgggg  | ctgag | ggcco | cc t  | gtgt | gata  | t tg  |      |      |      |      |      |      |        | 1602 |

| <210 | )> 1  | 14    |       |      |      |      |      |      |          |      |      |      |      |      |        |     |
|------|-------|-------|-------|------|------|------|------|------|----------|------|------|------|------|------|--------|-----|
| <21  | 1> 8  | 97    |       |      |      |      |      |      |          |      |      |      |      |      |        |     |
| <21  | 2> Di | NA    |       |      |      |      |      |      |          |      |      |      |      |      |        |     |
| <21: | 3> H  | omo : | sapi  | ens  |      |      |      |      |          |      |      |      |      |      |        |     |
| <220 | )>    |       |       |      |      |      |      |      |          |      |      |      |      |      |        |     |
| <22  | 1> C  | DS    |       |      |      |      |      |      |          |      |      |      |      |      |        |     |
| <222 | 2> (  | 99)   | (78   | 82)  |      |      |      |      |          |      |      |      |      |      |        |     |
| <400 | )> 1  | 14    |       |      |      |      |      |      |          |      |      |      |      |      |        |     |
| agto | cctc  | cca a | aagta | actt | gt g | tccg | ggtg | g tg | gact     | ggat | tcg  | ctgc | gga  | gccc | tggaag | 60  |
| ctg  | cctt  | tcc   | ttct  | ccct | gt g | ctta | acca | g ag | gtgc     | cc a | tg g | gt t | gg a | ca a | tg     | 113 |
|      |       |       |       |      |      |      |      |      |          | M    | et G | ly T | rp T | hr M | et     |     |
|      |       |       |       |      |      |      |      |      |          |      | l    | ÷    |      |      | 5      |     |
| agg  | ctg   | gtc   | aca   | gca  | gca  | ctg  | tta  | ctg  | ggt      | ctc  | atg  | atg  | gtg  | gtc  | act    | 161 |
| Arg  | Leu   | Val   | Thr   | Ala  | Ala  | Leu  | Leu  | Leu  | Gly      | Leu  | Met  | Met  | Val  | Val  | Thr    |     |
|      |       |       |       | 10   |      | -    |      |      | 15       |      |      |      |      | 20   |        |     |
| gga  | gac   | gag   | gat   | gag  | aac  | agc  | ccg  | tgt  | gcc      | cat  | gag  | gcc  | ctc  | ttg  | gac    | 209 |
| Gly  | Asp   | Glu   | Asp   | Glu  | Asn  | Ser  | Pro  | Cys  | Ala      | His  | Glu  | Ala  | Leu  | Leu  | Asp    |     |
|      |       |       | 25    |      |      |      |      | 30   |          |      |      |      | 35   |      |        |     |
| gag  | gac   | acc   | ctc   | ttt  | tgc  | cag  | ggc  | ctt  | gaa      | gtt  | ttc  | tac  | cca  | gag  | ttg    | 257 |
| Glu  | Asp   | Thr   | Leu   | Phe  | Cys  | Gln  | Gly  | Leu  | Glu      | Val  | Phe  | Tyr  | Pro  | Glu  | Leu    |     |
|      |       | 40    |       |      |      |      | 45   |      |          |      |      | 50   |      |      |        |     |
| ggg  | aac   | att   | ggc   | tgc  | aag  | gtt  | gtt  | cct  | gat      | tgt  | aac  | aac  | tac  | aga  | cag    | 305 |
| Gly  |       | Ile   | Gly   | Cys  | Lys  | Val  | Val  | Pro  | Asp      | Cys  | Asn  | Asn  | Tyr  | Arg  | Gln    |     |
|      | 55    |       |       |      |      | 60   |      | _    | ښر.<br>م | • •  | 65   |      |      |      |        |     |
| aag  | atc   | acc   | tcc   | tgg  | atg  | gag  | ccg  | ata  | gtc      | aag  | ttc  | ccg  | ggg  | gcc  | gtg    | 353 |

| Lys  | Ile | Thr  | Ser    | Trp  | Met        | Glu | Pro | He    | Val     | Lys | Phe | Pro | Gly | Ala   | Val  |     |
|------|-----|------|--------|------|------------|-----|-----|-------|---------|-----|-----|-----|-----|-------|------|-----|
| 70   |     |      | ÷      |      | <b>7</b> 5 |     |     |       |         | 80  |     |     |     |       | 85   |     |
| gac  | ggc | gca  | acc    | tat  | atc        | ctg | gtg | atg   | gtg     | gat | cca | gat | gcc | cct   | agc  | 401 |
| Asp  | Gly | Ala  | Thr,   | Tyr  | Ile        | Leu | Val | Met   | Val     | Asp | Pro | Asp | Ala | Pro   | Ser  |     |
|      |     |      |        | 90   |            |     |     |       | 95      |     |     |     |     | 100   |      |     |
| aga  | gca | gaa  | ccc    | aga  | cag        | aga | ttc | tgg   | aga     | cat | tgg | ctg | gta | aca   | gat  | 449 |
| Arg  | Λla | Glu  | Pro    | Arg  | G1n        | Arg | Phe | Trp   | Arg     | His | Trp | Leu | Val | Thr   | Asp  |     |
|      |     |      | 105    |      |            |     |     | 110   |         |     |     |     | 115 |       |      |     |
| atc  | aag | ggc  | gcc    | gac  | ctg        | aag | aaa | ggg   | aag     | att | cag | ggc | cag | gag   | tta  | 497 |
| Ile  | Lys | Gly  | Ala    | Asp  | Leu        | Lys | Lys | Gly   | Lys     | He  | Gln | Gly | Gln | Glu   | Leu  |     |
|      |     | 120  |        |      |            |     | 125 |       |         |     |     | 130 |     |       |      |     |
| tca  | gcc | tac  | cag    | gct  | ccc        | tcc | cca | ccg   | gca     | cac | agt | ggc | ttc | cat   | cgc  | 545 |
| Ser  |     | Tyr  | Gln    | Ala  | Pro        | Ser | Pro | Pro   | Ala     | His | Ser | Gly | Phe | His   | Arg  |     |
|      | 135 |      |        |      |            | 140 |     |       |         |     | 145 |     |     |       |      |     |
|      |     |      | ttt    |      |            |     |     |       |         |     |     |     |     |       |      | 593 |
|      | Gln | Phe  | Phe    | Val  |            | Leu | Gln | Glu   | Gly     |     | Val | He  | Ser | Leu   | Leu  |     |
| 150  |     |      |        |      | 155        |     |     |       |         | 160 |     |     |     |       | 165  |     |
|      |     |      | aac    |      |            |     |     |       |         |     |     |     |     |       | -    | 641 |
| Pro  | Lys | Glu  | Asn    |      | Thr        | Arg | Gly | Ser   |         | Lys | Meț | Asp | Arg |       | Leu  |     |
|      |     |      |        | 170  |            |     |     |       | 175     |     |     |     |     | 180   |      |     |
|      |     |      | cac    |      |            |     |     |       |         |     |     |     |     |       |      | 689 |
| Asn  | Arg | Phe  | His    | Leu  | Gly        | Glu | Pro |       | Ala     | Ser | Thr | Gln |     | Met   | Thr  |     |
|      |     |      | 185    |      |            |     |     | 190   |         |     |     |     | 195 |       |      |     |
|      |     |      | cag    |      |            |     |     |       | شرو     |     |     |     |     |       |      | 737 |
| 1117 | ASH | 1 Vr | 1. I D | a cn | \or        | rra | ınr | 1 017 | ( . I D | 412 | rrn | ura |     | u r a | 0.10 |     |

| 200                          | 205                 | 210                 |     |
|------------------------------|---------------------|---------------------|-----|
| agc gag ccc aag cac aaa aac  | cag gcg gag ata gc  | t gcc tgc t         | 780 |
| Ser Glu Pro Lys His Lys Asn  | Gln Ala Glu Ile Al  | a Ala Cys           |     |
| 215 220                      | 22                  | 5                   |     |
| agatagccgg ctttgccatc cgggca | tgtg gccacactgc cc  | accaccga cgatgtgggt | 840 |
| atggaacccc ctctggatac agaacc | cctt cttttccaaa ta  | aaaaaaaa atcatcc    | 897 |
|                              |                     |                     |     |
| <210> 115                    |                     |                     |     |
| <211> 1866                   |                     |                     |     |
| <212> DNA                    |                     |                     |     |
| <213> Homo sapiens           |                     |                     |     |
| ⟨220⟩                        |                     |                     |     |
| <221> CDS                    |                     |                     |     |
| <222> (142) (1467)           |                     |                     |     |
| <400> 115                    |                     |                     |     |
| gcccgcatgc gggggcgtgg cagtca | acag caacaaccca cad | cgccggca gggccagaaa | 60  |
| cteccatete ceteaceage eggaaa | gtac gagtcggctc ago | cctggagg gacccaacca | 120 |
| gagcctggcc tgggagccag g atg  | gcc atc cac aaa gco | c ttg gtg atg tgc   | 171 |
| Met                          | Ala Ile His Lys Ala | a Leu Val Met Cys   |     |
| 1                            | 5                   | 10                  |     |
| ctg gga ctg cct ctc ttc ctg  | ttc cca ggg gcc tgg | g gcc cag ggc cat   | 219 |
| Leu Gly Leu Pro Leu Phe Leu  | Phe Pro Gly Ala Trp | p Ala Gln Gly His   |     |
| 15                           | 20                  | 25                  |     |
| gtc cca ccc ggc tgc agc caa  | ggc ctc aac ccc ctو | g tac tac aac ctg   | 267 |
| Val Pro Pro Gly Cys Ser Gln  | Gly Leu Asn Pro Leu | u Tyr Tyr Asn Leu   | ÷   |

|     |     |     | 30  |     |     |            |     | 35  |     |     |     |     | 40  |     |     |   |     |
|-----|-----|-----|-----|-----|-----|------------|-----|-----|-----|-----|-----|-----|-----|-----|-----|---|-----|
| tgt | gac | cgc | tct | ggg | gcg | tgg        | ggc | atc | gtc | ctg | gag | gcc | gtg | gct | ggg |   | 315 |
| Cys | Asp | Arg | Ser | Gly | Ala | Trp        | Gly | He  | Val | Leu | Glu | Ala | Val | Ala | Gly |   |     |
|     |     | 45  |     |     |     |            | 50  |     |     |     |     | 55  |     |     |     |   |     |
| gcg | ggc | att | gtc | acc | acg | ttt        | gtg | ctc | acc | atc | atc | ctg | gtg | gcc | agc |   | 363 |
| Ala | Gly | Ile | Val | Thr | Thr | Phe        | Val | Leu | Thr | Ile | Ile | Leu | Val | Ala | Ser |   |     |
|     | 60  |     |     |     |     | <b>6</b> 5 |     |     |     |     | 70  |     |     |     |     |   |     |
| ctc | ccc | ttt | gtg | cag | gac | acc        | aag | aaa | cgg | agc | ctg | ctg | ggg | acc | cag |   | 411 |
| Leu | Pro | Phe | Val | Gln | Asp | Thr        | Lys | Lys | Arg | Ser | Leu | Leu | Gly | Thr | Gln |   |     |
| 75  |     |     |     |     | 80  |            |     |     |     | 85  |     |     |     |     | 90  |   |     |
| gta | ttc | ttc | ctt | ctg | ggg | acc        | ctg | ggc | ctc | ttc | tgc | ctc | gtg | ttt | gcc |   | 459 |
| Val | Phe | Phe | Leu | Leu | Gly | Thr        | Leu | Gly | Leu | Phe | Cys | Leu | Val | Phe | Ala |   |     |
|     |     |     |     | 95  |     |            |     |     | 100 |     |     |     |     | 105 |     |   |     |
| tgt | gtg | gtg | aag | ccc | gac | ttc        | tcc | acc | tgt | gcc | tct | cgg | cgc | ttc | ctc |   | 507 |
| Cys | Val | Val | Lys | Pro | Asp | Phe        | Ser | Thr | Cys | Ala | Ser | Arg | Arg | Phe | Leu |   |     |
|     |     |     | 110 |     |     |            |     | 115 |     |     |     |     | 120 |     |     |   |     |
| ttt | ggg | gtt | ctg | ttc | gcc | atc        | tgc | ttc | tct | tgt | ctg | gcg | gct | cac | gtc |   | 555 |
| Phe | Gly | Val | Leu | Phe | Ala | Ile        | Cys | Phe | Ser | Cys | Leu | Ala | Ala | His | Val |   |     |
|     |     | 125 |     |     |     |            | 130 |     |     |     |     | 135 |     |     |     |   |     |
| ttt | gcc | ctc | aac | ttc | ctg | gcc        | cgg | aag | aac | cac | ggg | ccc | cgg | ggc | tgg |   | 603 |
| Phe | Ala | Leu | Asn | Phe | Leu | Ala        | Arg | Lys | Asn | His | Gly | Pro | Arg | Gly | Trp |   |     |
|     | 140 |     |     |     |     | 145        |     |     |     |     | 150 |     |     |     |     |   |     |
| gtg | atc | ttc | act | gtg | gct | ctg        | ctg | ctg | acc | ctg | gta | gag | gtc | atc | atc |   | 651 |
| Val | He  | Phe | Thr | Val | Ala | Leu        | Leu | Leu | Thr | Leu | Val | Glu | Val | Ile | Ile | • |     |
| 155 |     |     |     |     | 160 |            |     | /   | _رړ | 165 |     |     |     |     | 170 |   |     |

| aat              | aca | gag | tgg | ctg | atc | atc | acc | ctg | gtt    | cgg | ggc | agt | ggc | gag | ggc | 699  |
|------------------|-----|-----|-----|-----|-----|-----|-----|-----|--------|-----|-----|-----|-----|-----|-----|------|
| Asn              | Thr | Glu | Trp | Leu | Ile | Ile | Thr | Leu | Val    | Arg | Gly | Ser | Gly | Glu | Gly |      |
|                  |     |     |     | 175 |     |     | •   |     | 180    |     |     |     |     | 185 |     |      |
| ggc              | cct | cag | ggc | aac | agc | agc | gca | ggc | tgg    | gcc | gtg | gcc | tcc | ссс | tgt | 747  |
| Gly              | Pro | Gln | Gly | Asn | Ser | Ser | Ala | Gly | Trp    | Ala | Val | Ala | Ser | Pro | Cys |      |
|                  |     |     | 190 |     |     |     |     | 195 |        |     |     |     | 200 |     |     |      |
| gcc              | atc | gcc | aac | atg | gac | ttt | gtc | atg | gca    | ctc | atc | tac | gtc | atg | ctg | 795  |
| Ala              | Ile | Ala | Asn | Met | Asp | Phe | Val | Met | Ala    | Leu | Ile | Tyr | Val | Met | Leu |      |
|                  |     | 205 |     |     |     |     | 210 |     |        |     |     | 215 |     |     |     |      |
| ctg              | ctg | ctg | ggt | gcc | ttc | ctg | ggg | gcc | tgg    | ccc | gcc | ctg | tgt | ggc | cgc | 843  |
| Leu              | Leu | Leu | Gly | Ala | Phe | Leu | Gly | Ala | Trp    | Pro | Ala | Leu | Cys | Gly | Arg |      |
|                  | 220 |     |     |     |     | 225 |     |     |        |     | 230 |     |     |     |     |      |
| tac              | aag | cgc | tgg | cgt | aag | cat | ggg | gtc | ttt    | gtg | ctc | ctc | acc | aca | gcc | 891  |
| Tyr              | Lys | Arg | Trp | Arg | Lys | His | Gly | Val | Phe    | Val | Leu | Leu | Thr | Thr | Ala |      |
| 235              |     |     |     |     | 240 |     |     |     |        | 245 |     |     |     |     | 250 |      |
| acc              | tcc | gtt | gcc | ata | tgg | gtg | gtg | tgg | atc    | gtc | atg | tat | act | tac | ggc | 939  |
| Thr              | Ser | Val | Ala | Ile | Trp | Val | Val | Trp | Ile    | Val | Met | Tyr | Thr | Tyr | Gly |      |
|                  |     |     |     | 255 |     |     |     |     | 260    |     |     |     |     | 265 |     |      |
| aac <sup>.</sup> | aag | cag | cac | aac | agt | ccc | acc | tgg | gat    | gac | ссс | acg | ctg | gcc | atc | 987  |
| Asn              | Lys | Gln | His | Asn | Ser | Pro | Thr | Trp | Asp    | Asp | Pro | Thr | Leu | Ala | Ile |      |
|                  |     |     | 270 |     |     |     |     | 275 |        |     |     |     | 280 |     |     |      |
| gcc              | ctc | gcc | gcc | aat | gcc | tgg | gcc | ttc | gtc    | ctc | ttc | tac | gtc | atc | ccc | 1035 |
| Ala              | Leu | Ala | Ala | Asn | Ala | Trp | Ala | Phe | Val    | Leu | Phe | Tyr | Val | Ile | Pro |      |
|                  |     | 285 |     |     |     |     | 290 | ,   | . شمور |     |     | 295 |     |     |     |      |
| gag              | gtc | tcc | cag | gtg | acc | aag | tcc | agc | cca    | gag | caa | agc | tac | cag | ggg | 1083 |

| Glu | Val | Ser | Gln | Val | Thr | Lys | Ser | Ser | Pro        | Glu | Gln | Ser | Tyr | Gln | Gly |       |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|------------|-----|-----|-----|-----|-----|-----|-------|
|     | 300 |     |     |     |     | 305 |     |     |            |     | 310 |     |     |     |     |       |
| gac | atg | tac | ссс | acc | cgg | ggc | gtg | ggc | tat        | gag | acc | atc | ctg | aaa | gag | 11,31 |
| Asp | Met | Tyr | Pro | Thr | Arg | Gly | Val | Gly | Tyr        | Glu | Thr | Ile | Leu | Lys | Glu |       |
| 315 |     |     |     |     | 320 |     |     |     |            | 325 |     |     |     |     | 330 |       |
| cag | aag | ggt | cag | agc | atg | ttc | gtg | gag | aac        | aag | gcc | ttt | tcc | atg | gat | 1179  |
| Gln | Lys | Gly | Gln | Ser | Met | Phe | Val | Glu | Asn        | Lys | Ala | Phe | Ser | Met | Asp |       |
|     |     |     |     | 335 |     |     |     |     | 340        |     |     |     |     | 345 |     |       |
| gag | ccg | gtt | gca | gct | aag | agg | ccg | gtg | tca        | cca | tac | agc | ggg | tac | aat | 1227  |
| Glu | Pro | Val | Ala | Ala | Lys | Arg | Pro | Val | Ser        | Pro | Tyr | Ser | Gly | Tyr | Asn |       |
|     |     |     | 350 |     |     |     |     | 355 |            |     |     |     | 360 |     |     |       |
| ggg | cag | ctg | ctg | acc | agt | gtg | tac | cag | ccc        | act | gag | atg | gcc | ctg | atg | 1275  |
| Gly | Gln | Leu | Leu | Thr | Ser | Val | Tyr | G1n | Pro        | Thr | Glu | Met | Ala | Leu | Met |       |
|     |     | 365 |     |     |     |     | 370 |     |            |     |     | 375 |     |     |     |       |
| cac | aaa | gtt | ccg | tcc | gaa | gga | gct | tac | gac        | atc | atc | ctc | cca | cgg | gcc | 1323  |
| His | Lys | Val | Pro | Ser | Glu | Gly | Ala | Tyr | Asp        | Ile | Ile | Leu | Pro | Arg | Ala |       |
|     | 380 |     |     |     |     | 385 |     |     |            |     | 390 |     |     |     |     |       |
| acc | gcc | aac | agc | cag | gtg | atg | ggc | agt | gcc        | aac | tcg | acc | ctg | cgg | gct | 1371  |
| Thr | Ala | Asn | Ser | Gln | Val | Met | Gly | Ser | Ala        | Asn | Ser | Thr | Leu | Arg | Ala |       |
| 395 |     |     |     |     | 400 |     |     |     |            | 405 |     |     |     |     | 410 |       |
| gaa | gac | atg | tac | tcg | gcc | cag | agc | cac | cag        | gcg | gcc | aca | ccg | ccg | aaa | 1419  |
| Glu | Asp | Met | Tyr | Ser | Ala | Gln | Ser | His | Gln        | Ala | Ala | Thr | Pro | Pro | Lys |       |
|     |     |     |     | 415 |     |     |     |     | 420        |     |     |     |     | 425 |     |       |
| gac | ggc | aag | aac | tct | cag | gtc | ttt | aga | aac<br>ند. | ccc | tac | gtg | tgg | gac |     | 1464  |
| Asp | Glv | Lvs | Asn | Ser | Gln | Val | Phe | Aro | Asn        | Pro | Tvr | Val | Trn | Asn |     |       |

| 430                     | 435                   | 440                   |      |
|-------------------------|-----------------------|-----------------------|------|
| tgagtc agcggtggcg aggag | gaggcg gtcggatttg ggg | agggccc tgaggacctg    | 1520 |
| gccccgggca agggactete   | caggeteete eteceeetgg | caggeceage aacatgtgee | 1580 |
| ccagatgtgg aagggcctcc   | ctctctgcca gtgtttgggt | gggtgtcatg ggtgtcccca | 1640 |
| cccactcctc agtgtttgtg g | gagtegagga gecaacecea | gcctcctgcc aggatcacct | 1700 |
| cggcggtcac actccagcca a | natagtgttc tcggggtggt | ggctgggcag cgcctatgtt | 1760 |
| tetetggaga tteetgeaac o | ctcaagagac ttcccaggcg | ctcaggcctg gatcttgctc | 1820 |
| ctctgtgagg aacaagggtg o | cctaataaat acatttctgc | tttatt                | 1866 |
|                         |                       |                       |      |
| <210> 116               |                       |                       |      |
| <211> 2198              |                       |                       |      |
| <212> DNA               |                       |                       |      |
| <213> Homo sapiens      |                       |                       |      |
| ⟨220⟩                   |                       |                       |      |
| <221> CDS               |                       |                       |      |
| 〈222〉(50) (847)         |                       |                       |      |
| <400> 116               |                       |                       |      |
| aaaatggcgt agagcctagc a | acagegeag geteceagee  | gagtccgtt atg gcc     | 55   |
|                         |                       | Met Ala               | •    |
|                         |                       | 1                     | •    |
| gct gcc gtc ccg aag agg | atg agg ggg cca gca   | caa gcg aaa ctg ctg   | 103  |
| Ala Ala Val Pro Lys Arg | Met Arg Gly Pro Ala   | Gln Ala Lys Leu Leu   |      |
| 5                       | 10                    | 15                    |      |
| ccc ggg tcg gcc atc caa | gcc ctt gtg ggg ttg   | gcg cgg ccg ctg gtc   | 151  |
| Pro Gly Ser Ala Ile Gln | Ala Leu Val Gly Leu   | Ala Arg Pro Leu Val   |      |

|     | 20  |      |     |     |     | 25  |     |     |     |     | 30  |     |     |     |     |     |
|-----|-----|------|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
| ttg | gcg | ctc  | ctg | ctt | gtg | tcc | gcc | gct | cta | tcc | agt | gtt | gta | tca | cgg | 199 |
| Leu | Ala | Leu  | Leu | Leu | Val | Ser | Ala | Ala | Leu | Ser | Ser | Val | Val | Ser | Arg |     |
| 35  |     |      |     |     | 40  |     |     |     |     | 45  |     |     |     |     | 50  |     |
| act | gat | tca  | ccg | agc | cca | acc | gta | ctc | aac | tca | cat | att | tct | acc | cca | 247 |
| Thr | Asp | Ser  | Pro | Ser | Pro | Thr | Val | Leu | Asn | Ser | His | Ile | Ser | Thr | Pro |     |
|     |     |      |     | 55  |     |     |     |     | 60  |     |     |     |     | 65  |     |     |
| aat | gtg | aat  | gct | tta | aca | cat | gaa | aac | caa | acc | aaa | cct | tct | att | tcc | 298 |
| Asn | Val | Asn  | Ala | Leu | Thr | His | Glu | Asn | Gln | Thr | Lys | Pro | Ser | Ile | Ser |     |
|     |     |      | 70  |     |     |     |     | 75  |     |     |     |     | 80  |     |     |     |
| caa | atc | agc  | acc | acc | ctc | cct | ccc | acg | acg | agt | acc | aag | aaa | agt | gga | 343 |
| Gln | He  | Ser  | Thr | Thr | Leu | Pro | Pro | Thr | Thr | Ser | Thr | Lys | Lys | Ser | Gly |     |
|     |     | 85   |     |     |     |     | 90  |     |     |     |     | 95  |     |     |     |     |
| gga | gca | tct  | gtg | gtc | cct | cat | ccc | tcg | cct | act | cct | ctg | tct | caa | gag | 391 |
| Gly | Ala | Ser  | Val | Val | Pro | His | Pro | Ser | Pro | Thr | Pro | Leu | Ser | Gln | Glu |     |
|     | 100 |      |     |     |     | 105 |     |     |     |     | 110 |     |     |     |     |     |
| gaa | gct | gat  | aac | aat | gaa | gat | cct | agt | ata | gag | gag | gag | gat | ctt | ctc | 439 |
| Glu | Ala | Asp  | Asn | Asn | Glu | Asp | Pro | Ser | Ile | Glu | Glu | Glu | Asp | Leu | Leu |     |
| 115 |     |      |     |     | 120 |     |     |     |     | 125 |     |     |     |     | 130 |     |
| atg | ctg | aac  | agt | tct | cca | tcc | aca | gcc | aaa | gac | act | cta | gac | aat | ggc | 487 |
| Met | Leu | Asn  | Ser | Ser | Pro | Ser | Thr | Ala | Lys | Asp | Thr | Leu | Asp | Asn | Gly |     |
|     |     |      |     | 135 |     |     |     |     | 140 |     |     |     |     | 145 |     |     |
| gat | tat | gga  | gaa | cca | gac | tat | gac | tgg | acc | acg | ggc | ccc | agg | gac | gac | 539 |
| Asp | Tyr | G1 y | Glu | Pro | Asp | Tyr | Asp | Trp | Thr | Thr | Gly | Pro | Arg | Asp | Asp |     |
|     |     |      | 150 |     |     |     |     | 155 | ,   |     |     |     | 160 |     |     |     |

| gac  | gag   | tct   | gat   | gac   | acc   | ttg   | gaa   | gaa   | aac   | agg   | ggt   | tac   | atg           | gaa   | att    | 583  |
|------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|---------------|-------|--------|------|
| Asp  | Glu   | Ser   | Asp   | Asp   | Thr   | Leu   | Glu   | Glu   | Asn   | Arg   | Gly   | Tyr   | Met           | Glu   | Ile    |      |
|      |       | 165   |       |       |       |       | 170   |       |       |       |       | 175   |               |       |        |      |
| gaa  | cag   | tca   | gtg   | aaa   | tct   | ttt   | aag   | atg   | cca   | tcc   | tca   | aat   | ata           | gaa   | gag    | 631  |
| Glu  | Gln   | Ser   | Val   | Lys   | Ser   | Phe   | Lys   | Met   | Pro   | Ser   | Ser   | Asn   | Ile           | Glu   | Glu    |      |
|      | 180   |       |       |       |       | 185   |       |       |       |       | 190   |       |               |       |        |      |
| gaa  | gac   | agc   | cat   | ttc   | ttt   | ttt   | cat   | ctt   | att   | att   | ttt   | gct   | ttt           | tgc   | att    | 679  |
| Glu  | Asp   | Ser   | His   | Phe   | Phe   | Phe   | His   | Leu   | Ile   | Ile   | Phe   | Ala   | Phe           | Cys   | Ile    |      |
| 195  |       |       |       |       | 200   |       |       |       |       | 205   |       |       |               |       | 210    |      |
| gct  | gtt   | gtt   | tac   | att   | aca   | tat   | cac   | aac   | aaa   | agg   | aag   | att   | ttt           | ctt   | ctg    | 727  |
| Ala  | Val   | Val   | Tyr   | Ile   | Thr   | Tyr   | His   | Asn   | Lys   | Arg   | Lys   | Ile   | Phe           | Leu   | Leu    |      |
|      |       |       |       | 215   |       |       |       |       | 220   |       |       |       |               | 225   |        |      |
| gtt  | caa   | agc   | agg   | aaa   | tgg   | cgt   | gat   | ggc   | ctt   | tgt   | tcc   | aaa   | aca           | gtg   | gaa    | 775  |
| Val  | Gln   | Ser   | Arg   | Lys   | Trp   | Arg   | Asp   | Gly   | Leu   | Cys   | Ser   | Lys   | Thr           | Val   | Glu    |      |
|      |       |       | 230   |       |       |       |       | 235   |       |       |       |       | 240           |       |        |      |
| tac  | cat   | cgc   | cta   | gat   | cag   | aat   | gtt   | aat   | gag   | gca   | atg   | cct   | tct           | ttg   | aag    | 823  |
| Tyr  | His   | Arg   | Leu   | Asp   | Gln   | Asn   | Val   | Asn   | Glu   | Ala   | Met   | Pro   | Ser           | Leu   | Lys    |      |
|      |       | 245   |       |       |       |       | 250   |       |       |       |       | 255   |               |       |        |      |
| att  | acc   | aat   | gat   | tat   | att   | ttt   | taaa  | agc a | actg  | tgati | tt ga | aatti | tgct          | t     | ,      | 870  |
| Ile  | Thr   | Asn   | Asp   | Tyr   | Ile   | Phe   |       |       |       |       |       |       |               |       |        |      |
|      | 260   |       |       |       |       | 265   |       |       |       |       |       |       |               |       |        |      |
| atgi | taati | ttt a | attte | gcttg | ga ci | tttti | tatai | t gat | tattı | gtgc  | aaat  | tgtti | tgc (         | cata  | ggcaat | 930  |
| tggt | tacti | taa a | atgag | gaggi | tg ag | gtcto | eteti | t ttg | gccti | tggt  | gcti  | ttgga | aaa           | ttaaa | atgtca | 990  |
| caaa | acga  | gta 1 | tataa | attti | tt ta | atcte | gtaci | t tti | tagaا | gctg  | agti  | taat  | tca           | ggtg  | tccaaa | 1050 |
| atgi | tgagt | tta a | aacat | ttaco | et ta | atati | ttaca | a cti | gtta  | gttt  | ttai  | ttgti | t <b>tt</b> : | agati | ttatta | 1110 |

| tgcttcttct | ggaagtatta | gtgatgctac | ttttaaaaaga | teccaaaett | gtaactaaat | 1170 |
|------------|------------|------------|-------------|------------|------------|------|
| tctgacatat | ctgttactgc | tgactcacat | tcattctccg  | ccattcaaat | actattttt  | 1230 |
| atccacattt | ttttttgttc | ccaaactgta | atgtacaagg  | atatgtgtga | taatgctttg | 1290 |
| gatttgagta | atatttttt  | ttcttccaag | aaaactgctt  | tggatatttt | tagataattt | 1350 |
| aaacataatt | taggataatg | atattgctca | atctgaccac  | aattttaggt | aaaacattaa | 1410 |
| atgtgtcaag | aaatcttggc | aacagagact | ctgcagettg  | cagtggacat | agataaaatg | 1470 |
| ttacagagat | actattttt  | tggttggaat | tactatatta  | aatttagaag | cagaaactgg | 1530 |
| taaaatgtta | aatacatgta | caattgcttt | tagttagcaa  | ttgattgtag | catgggttcc | 1590 |
| tccaaggttt | caagcaatgg | gcagagttta | aaattatatc  | agattcgttt | acttcgttta | 1650 |
| ttattttaca | gtaaatttga | ataaatctta | ggggtcatta  | tcacttaaat | aatactgtac | 1710 |
| ctaggtcttt | caaattaaaa | ttatacctga | atgaagttgt  | ttgtatacat | aaaggatatt | 1770 |
| tgtgtacaat | tacctttttt | ccccacact  | tgttttcttt  | gtttttgttt | tttatggcaa | 1830 |
| ctggaaagta | tttactatgg | gattcattta | tgtctgtctt  | tctatcataa | agaattgatc | 1890 |
| aatatgtaaa | tatgtgattt | gaaccatggt | tgacttacaa  | gtgtcactac | agctttttag | 1950 |
| aaaacatagc | cctaatatat | gttaagcagg | accegggtga  | gccagtgggc | ttgcgcttta | 2010 |
| tgtagagctg | gaagaaggcc | gtccatcctg | tctcttgggc  | ggacagtgta | ctttcctaat | 2070 |
| agggaaggga | agcacaatgg | aaatacccct | gaaccgtttt  | attgcagtaa | tttttttcat | 2130 |
| atctgaaact | attatttaat | attttgaata | agattttaaa  | aaataaatgg | caaagatata | 2190 |
| aatctatg   |            |            |             |            |            | 2198 |

<210> 117

<211> 2180

<212> DNA

<213> Homo sapiens

<220>

| <22 | 1> C | DS    |       |      |       |      |      |       |       |       |       |      |      |       |       |      |
|-----|------|-------|-------|------|-------|------|------|-------|-------|-------|-------|------|------|-------|-------|------|
| <22 | 2> ( | 69).  | (69   | 95)  |       |      |      |       |       |       |       |      |      |       |       |      |
| <40 | 0> 1 | 17    |       |      |       |      |      |       |       |       |       |      |      |       |       |      |
| aac | cagc | gcc ( | gcgga | acac | cg g  | cacc | ggcg | c ca  | cgga  | ctcc  | gca   | ggac | ccc  | gcgc  | cegee | g 60 |
| ccg | ccgc | t at  | g ct  | g gg | g ct  | g ct | g gt | g gc  | g tt  | g ct  | g gc  | c ct | g gg | g ct  | c gct | 110  |
|     |      | Me    | t Lei | ı Gl | y Lei | u Le | u Va | 1 A1: | a Lei | u Lei | u Ala | a Le | u Gl | y Lei | ı Ala | •    |
|     |      |       | 1     |      |       | :    | 5    |       |       |       | 10    | D .  |      |       |       |      |
| gtc | ttt  | gcg   | ctg   | ctg  | gac   | gtc  | tgg  | tac   | ctg   | gtg   | cgc   | ctt  | ccg  | tgc   | gcc   | 158  |
| Val | Phe  | Ala   | Leu   | Leu  | Asp   | Val  | Trp  | Tyr   | Leu   | Val   | Arg   | Leu  | Pro  | Cys   | Ala   |      |
| 15  |      |       |       |      | 20    |      |      |       |       | 25    |       |      |      |       | 30    |      |
| gtg | ctg  | cgc   | gcg   | cgc  | ctg   | ctg  | cag  | ccg   | cgc   | gtc   | cgt   | gac  | ctg  | cta   | gct   | 206  |
| Val | Leu  | Arg   | Ala   | Arg  | Leu   | Leu  | Gln  | Pro   | Arg   | Val   | Arg   | Asp  | Leu  | Leu   | Ala   |      |
|     |      |       |       | 35   |       |      |      |       | 40    |       |       |      |      | 45    |       |      |
| gag | cag  | cgc   | ttc   | ccg  | ggc   | cgc  | gtg  | ctg   | ссс   | tcg   | gac   | ttg  | gac  | ctg   | ctg   | 254  |
| Glu | Gln  | Arg   | Phe   | Pro  | Gly   | Arg  | Val  | Leu   | Pro   | Ser   | Asp   | Leu  | Asp  | Leu   | Leu   |      |
|     |      |       | 50    |      |       |      |      | 55    |       |       |       |      | 60   |       |       |      |
| ttg | cac  | atg   | aac   | aac  | gcg   | cgc  | tac  | ctg   | cgc   | gag   | gcc   | gac  | ttt  | gcg   | cgc   | 302  |
| Leu | His  | Met   | Asn   | Asn  | Ala   | Arg  | Tyr  | Leu   | Arg   | Glu   | Ala   | Asp  | Phe  | Ala   | Arg   |      |
|     |      | 65    |       |      |       |      | 70   |       | •     |       |       | 75   |      |       |       |      |
| gtc | gcg  | cac   | ctg   | acc  | cgc   | tgc  | ggg  | gtg   | ctc   | ggg   | gcg   | ctg  | agg  | gag   | ttg   | 350  |
| Val | Ala  | His   | Leu   | Thr  | Arg   | Cys  | Gly  | Val   | Leu   | Gly   | Ala   | Leu  | Arg  | Glu   | Leu   |      |
|     | 80   |       |       |      |       | 85   |      |       |       |       | 90    |      |      |       |       |      |
| cgg | gcg  | cac   | acg   | gtg  | ctg   | gcg  | gcc  | tcg   | tgc   | gcg   | cgc   | cac  | cgc  | cgc   | tcg   | 398  |
| Arg | Ala  | His   | Thr   | Val  | Leu   | Ala  | Ala  | Ser   | Cys   | Ala   | Arg   | His  | Arg  | Arg   | Ser   |      |
| 95  |      |       |       |      | 100   |      |      | /     | •     | 105   |       |      |      |       | 110   |      |

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| ctg | cgc  | ctg   | ctg  | gag  | ccc  | ttc  | gag  | gtg  | cgc        | acc  | cgc  | ctg  | ctg  | ggc  | tgg    | 446  |
|-----|------|-------|------|------|------|------|------|------|------------|------|------|------|------|------|--------|------|
| Leu | Arg  | Leu   | Leu  | Glu  | Pro  | Phe  | Glu  | Val  | Arg        | Thr  | Arg  | Leu  | Leu  | Gly  | Trp    |      |
|     |      |       |      | 115  |      |      | •    |      | 120        |      |      |      |      | 125  |        |      |
| gac | gac  | cgc   | gcg  | ttc  | tac  | ctg  | gag  | gcg  | cgc        | ttt  | gtc  | agc  | ctg  | cgg  | gac    | 494  |
| Asp | Asp  | Arg   | Ala  | Phe  | Tyr  | Leu  | Glu  | Ala  | Arg        | Phe  | Val  | Ser  | Leu  | Arg  | Asp    |      |
|     |      |       | 130  |      |      |      |      | 135  |            |      |      |      | 140  |      |        |      |
| ggt | ttc  | gtg   | tgc  | gcg  | ctg  | ctg  | cgc  | ttc  | cgg        | cag  | cac  | ctg  | ctg  | ggc  | acc    | 542  |
| Gly | Phe  | Val   | Cys  | Ala  | Leu  | Leu  | Arg  | Phe  | Arg        | Gln  | His  | Leu  | Leu  | Gly  | Thr    |      |
|     |      | 145   |      |      |      |      | 150  |      |            |      |      | 155  |      |      |        |      |
| tca | ccc  | gag   | cgc  | gtc  | gtg  | cag  | cac  | ctg  | tgc        | cag  | cgc  | agg  | gtg  | gag  | ccc    | 590  |
| Ser | Pro  | Glu   | Arg  | Val  | Val  | Gln  | His  | Leu  | Cys        | Gln  | Arg  | Arg  | Val  | Glu  | Pro    |      |
|     | 160  |       |      |      |      | 165  |      |      | •          |      | 170  | •    |      |      |        |      |
| cct | gag  | ctg   | ccc  | gct  | gat  | ctg  | cag  | cac  | tgg        | atc  | tcc  | tac  | aac  | gag  | gcc    | 638  |
| Pro | Glu  | Leu   | Pro  | Ala  | Asp  | Leu  | Gln  | His  | Trp        | Ile  | Ser  | Tyr  | Asn  | Glu  | Ala    |      |
| 175 |      |       |      |      | 180  |      |      |      |            | 185  |      |      |      |      | 190    |      |
| agc | agc  | cag   | ctg  | ctc  | cgc  | atg  | gag  | agt  | ggg        | ctc  | agt  | gat  | gtc  | acc  | aag    | 686  |
| Ser | Ser  | Gln   | Leu  | Leu  | Arg  | Met  | Glu  | Ser  | Gly        | Leu  | Ser  | Asp  | Val  | Thṛ  | Lys    |      |
|     |      |       |      | 195  |      |      |      |      | 200        |      |      |      |      | 205  |        |      |
| gac | cag  | tga   | ccgc | c ac | cttc | acac | cgt  | ctgc | cct        | ggcc | acca | tc c | tggg | cctg | g      | 740  |
| Asp | Gln  |       |      |      |      |      |      |      |            |      |      |      |      |      |        |      |
| ggg | ctgc | cca   | caga | tggg | ca g | tctc | agcc | a ta | ctct       | gttc | cag  | ctgg | agt  | agcc | tcctga | 800  |
| cca | gcct | ggc   | ccac | cctg | ct c | cacc | cact | g gg | cccc       | ccca | gtt  | attg | ata  | cccc | tctgtg | 860  |
| ctg | ggct | cca   | cgct | aggc | ag a | agga | ggag | t gg | catt       | ggca | tcc  | tgac | сса  | gctc | tgccct | 920  |
| caa | ggtg | ggg : | atgg | atgg | gc a | aagg | agag | t cc | tgcc       | tggc | cct  | acga | tga  | ggcc | actcat | 980  |
| gtg | ggcc | tag   | gtag | ggga | gg a | tggt | gcct | g gá | ے۔<br>gcag | aggg | acc  | caca | agt  | gcct | cccgag | 1040 |

| cctagatcct | ggctcggacc | actgcaaggg | ccgaggcagg | gccagaccag | agcatcctgg | 1100 |
|------------|------------|------------|------------|------------|------------|------|
| gtacaggcct | gggctctcca | gggcctgggc | ctgattcagg | tgcagtgggc | actectgaag | 1160 |
| ggtcagagcg | gcatctgcca | ggcagcccct | ctggcttccg | ctgaggtggt | tgcaggcctg | 1220 |
| gggcagagcc | tgggtggtca | gaggccgggg | ctagaggcag | atggaaggga | ggcatttgct | 1280 |
| gacagaggac | ggggcacccg | ggctcccact | gcagtcggcc | ttgcctcctc | ctcctct    | 1340 |
| acctccagtc | aggctggacg | ggagggtagc | cttgtggctg | agaggggtca | gactaggtgg | 1400 |
| cacaggggct | cctggaaaga | cagcaggett | cctgctgggc | gttcccttgt | tggagggaat | 1460 |
| agagtggggg | tgggactctg | caggggtgtc | cttgtccact | cgcacccctc | gccgcccacc | 1520 |
| agggccatgc | tctgtgactt | gggctgatcc | ccaccctttc | tgggcctaca | gcaccacagg | 1580 |
| ccgctgtacc | cccttagagc | tgccctctc  | tggcctggcc | ggcagacgtc | ttcttaactc | 1640 |
| ctctgtcctc | tatattcagc | atgttccttg | tcagctgctg | ggccggccct | gccttgcgct | 1700 |
| agcagagcct | ctcctggcag | cttctcaggt | ctccctaatg | gagacaccag | gctactagga | 1760 |
| cactggctgg | ggccaccccc | tcctgcctaa | tgcctcacct | tacagctggg | gaaactgagg | 1820 |
| cctggaatgg | cccagagtca | ccaaggcaaa | gttggggctg | gtcccagcct | gaggetecag | 1880 |
| ctgatgccct | cagctcccag | agagggggtg | ccccatctag | ctgggtgcag | gggtcactgc | 1940 |
| ttgtcagctc | agggccctgt | gcccgcttgc | ctgttcccct | acatctgtgc | ctgcacatcc | 2000 |
| agaactgcct | ccttgccgct | gcctccagga | agcccacctt | gagccagagt | caagggctgc | 2060 |
| agcactgccc | gatagaacac | gcccgccctc | actgctgttc | ttgccttaca | gccaccatgg | 2120 |
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<211> 1527

<212> DNA

<213> Homo sapiens

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| agto | ettec | cag | ggcgg | gcgg1 | tg gg | gtgto | ecgci | t tct | ctct  | tgct | ctto | egaet | tgc a | accgo | cactc | g 60 |
| cgcg | gtgad | ссс | tgact | tccc  | ec ta | agtca | gcto  | c ago | eggte | gctg | cc a | atg g | gcg 1 | tgg ( | egg   | 114  |
|      |       |     |       |       |       |       |       |       |       |      | N    | let / | \la î | Trp / | Arg   |      |
|      |       |     |       |       |       |       |       |       |       |      |      | 1     |       |       |       |      |
| cgg  | cgc   | gaa | gcc   | agc   | gtc   | ggg   | gct   | cgc   | ggc   | gtg  | ttg  | gct   | ctg   | gcg   | ttg   | 162  |
| Arg  | Arg   | Glu | Ala   | Ser   | Val   | Gly   | Ala   | Arg   | Gly   | Val  | Leu  | Ala   | Leu   | Ala   | Leu   |      |
| 5    |       |     |       |       | 10    |       |       |       |       | 15   |      |       |       |       | 20    |      |
| ctc  | gcc   | ctg | gcc   | ctg   | tgc   | gtg   | ccc   | ggg   | gcc   | cgg  | ggc  | cgg   | gct   | ctc   | gag   | 210  |
| Leu  | Ala   | Leu | Ala   | Leu   | Cys   | Val   | Pro   | Gly   | Ala   | Arg  | Gly  | Arg   | Ala   | Leu   | Glu   |      |
|      |       |     |       | 25    |       |       |       |       | 30    |      |      |       |       | 35    |       |      |
| tgg  | ttc   | tcg | gcc   | gtg   | gta   | aac   | atc   | gag   | tac   | gtg  | gac  | ccg   | cag   | acc   | aac   | 258  |
| Trp  | Phe   | Ser | Ala   | Val   | Val   | Asn   | Ile   | Glu   | Tyr   | Val  | Asp  | Pro   | Gln   | Thr   | Asn   |      |
|      |       |     | 40    |       |       |       |       | 45    |       |      |      |       | 50    |       |       |      |
| ctg  | acg   | gtg | tgg   | agc   | gtc   | tcg   | gag   | agt   | ggc   | cgc  | ttc  | ggc   | gac   | agc   | tcg   | 306  |
| Leu  | Thr   | Val | Trp   | Ser   | Val   | Ser   | Glu   | Ser   | Gly   | Arg  | Phe  | Gly   | Asp   | Ser   | Ser   |      |
|      |       | 55  |       |       |       |       | 60    |       |       |      |      | 65    |       |       |       |      |
| ccc  | aag   | gag | ggc   | gcg   | cat   | ggc   | ctg   | gtg   | ggc   | gtc  | ccg  | tgg   | gcg   | ccc   | ggc   | 354  |
| Pro  | Lys   | Glu | Gly   | Ala   | His   | Gly   | Leu   | Val   | Gly   | Val  | Pro  | Trp   | Ala   | Pro   | Gly   |      |
|      | 70    |     |       |       |       | 75    |       |       |       |      | 80   |       |       |       |       |      |
| gga  | gac   | ctc | gag   | ggc   | tgc   | gcg   | ccc   | gac   | acg   | cgc  | ttc  | ttc   | gtg   | ccc   | gag   | 402  |
| Gly  | Asp   | Leu | Glu   | Gly   | Cys   | Ala   | Pro   | Asp   | Thr   | Arg  | Phe  | Phe   | Val   | Pro   | Glu   |      |
| 85   |       |     |       |       | 90    |       |       | /     |       | 95   |      |       |       |       | 100   |      |

| ссс | ggc | ggc | cga | ggg | gcc | gcg | ccc | tgg | gtc    | gcc | ctg | gtg | gct | cgt | ggg | 450 |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|--------|-----|-----|-----|-----|-----|-----|-----|
| Pro | Gly | Gly | Arg | Gly | Ala | Ala | Pro | Trp | Val    | Ala | Leu | Val | Ala | Arg | Gly |     |
|     |     |     |     | 105 |     |     |     |     | 110    |     |     |     |     | 115 |     |     |
| ggc | tgc | acc | ttc | aag | gac | aag | gtg | ctg | gtg    | gcg | gcg | cgg | agg | aac | gcc | 498 |
| Gly | Cys | Thr | Phe | Lys | Asp | Lys | Val | Leu | Val    | Ala | Ala | Arg | Arg | Asn | Ala |     |
|     |     |     | 120 |     |     |     |     | 125 |        |     |     |     | 130 |     |     |     |
| tcg | gcc | gtc | gtc | ctc | tac | aat | gag | gag | cgc    | tac | ggg | aac | atc | acc | ttg | 546 |
| Ser | Ala | Val | Val | Leu | Tyr | Asn | Glu | Glu | Arg    | Tyr | Gly | Asn | Ile | Thr | Leu |     |
|     |     | 135 |     |     |     |     | 140 |     |        |     |     | 145 |     |     |     |     |
| ссс | atg | tct | cac | gcg | gga | aca | gga | aat | ata    | gtg | gtc | att | atg | att | agc | 594 |
| Pro | Met | Ser | His | Ala | Gly | Thr | Gly | Asn | Ile    | Val | Val | Ile | Met | Ile | Ser |     |
|     | 150 |     |     |     |     | 155 |     |     |        |     | 160 |     |     |     |     |     |
| tat | cca | aaa | gga | aga | gaa | att | ttg | gag | ctg    | gtg | caa | aaa | gga | att | cca | 642 |
| Tyr | Pro | Lys | Gly | Arg | Glu | Ile | Leu | Glu | Leu    | Val | Gln | Lys | Gly | Ile | Pro |     |
| 165 |     |     |     |     | 170 |     |     |     |        | 175 |     |     |     |     | 180 |     |
| gta | acg | atg | acc | ata | ggg | gtt | ggc | acc | cgg    | cat | gta | cag | gag | ttc | atc | 690 |
| Val | Thr | Met | Thr | Ile | G1y | Val | Gly | Thr | Arg    | His | Val | Gln | Glu | Phe | Ile |     |
|     |     |     |     | 185 |     |     |     |     | 190    |     |     |     |     | 195 |     |     |
| agc | ggt | cag | tct | gtg | gtg | ttt | gtg | gcc | att    | gcc | ttc | atc | acc | atg | atg | 738 |
| Ser | Gly | Gln | Ser | Val | Val | Phe | Val | Ala | Ile    | Ala | Phe | Ile | Thr | Met | Met |     |
|     |     |     | 200 |     |     |     |     | 205 |        |     |     |     | 210 |     |     |     |
| att | atc | tcg | tta | gcc | tgg | cta | ata | ttt | tac    | tat | ata | cag | cgt | ttc | cta | 786 |
| Ile | Ile | Ser | Leu | Ala | Trp | Leu | Ile | Phe | Tyr    | Tyr | Île | Gln | Arg | Phe | Leu |     |
|     |     | 215 |     |     |     |     | 220 |     | ۰۰ شمه |     |     | 225 |     |     |     |     |
| tat | act | ggc | tct | cag | att | gga | agt | cag | agc    | cat | aga | aaa | gaa | act | aag | 834 |

| Tyr | Thr | Gly | Ser | Gln | Ile | Gly | Ser | Gln | Ser | His | Arg | Lys | Glu | Thr | Lys |      |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|------|
|     | 230 |     |     |     |     | 235 |     |     |     |     | 240 |     |     |     |     |      |
| aaa | gtt | att | ggc | cag | ctt | cta | ctt | cat | act | gta | aag | cat | gga | gaa | aag | 882  |
| Lys | Val | Ile | Gly | Gln | Leu | Leu | Leu | His | Thr | Vai | Lys | His | Gly | Glu | Lys |      |
| 245 |     |     |     |     | 250 |     |     |     |     | 255 |     |     |     |     | 260 |      |
| gga | att | gat | gtt | gat | gct | gaa | aat | tgt | gca | gtg | tgt | att | gaa | aat | ttc | 930  |
| Gly | Ile | Asp | Val | Asp | Ala | Glu | Asn | Cys | Ala | Val | Cys | Ile | Glu | Asn | Phe |      |
|     |     |     |     | 265 |     |     |     |     | 270 |     |     |     |     | 275 |     |      |
| aaa | gta | aag | gat | att | att | aga | att | ctg | cca | tgc | aag | cat | att | ttt | cat | 978  |
| Lys | Val | Lys | Asp | Ile | Ile | Arg | Ile | Leu | Pro | Cys | Lys | His | Ile | Phe | His |      |
|     |     |     | 280 |     |     |     |     | 285 |     |     |     |     | 290 |     |     |      |
| aga | ata | tgc | att | gac | cca | tgg | ctt | ttg | gat | cac | cga | aca | tgt | cca | atg | 1026 |
| Arg | He  | Cys | He  | Asp | Pro | Trp | Leu | Leu | Asp | His | Arg | Thr | Cys | Pro | Met |      |
|     |     | 295 |     |     |     |     | 300 |     |     |     |     | 305 |     |     |     |      |
| tgt | aaa | ctt | gat | gtc | atc | aaa | gcc | cta | gga | tat | tgg | gga | gag | cct | ggg | 1074 |
| Cys | Lys | Leu | Asp | Val | He  | Lys | Ala | Leu | Gly | Tyr | Trp | Gly | Glu | Pro | Gly |      |
|     | 310 |     |     |     |     | 315 |     |     |     |     | 320 |     |     |     |     |      |
| gat | gta | cag | gag | atg | cct | gct | cca | gaa | tct | cct | cct | gga | agg | gat | cca | 1122 |
| Asp | Val | Gln | Glu | Met | Pro | Ala | Pro | Glu | Ser | Pro | Pro | Gly | Arg | Asp | Pro |      |
| 325 |     |     |     |     | 330 |     |     |     |     | 335 |     |     |     |     | 340 |      |
| gct | gca | aat | ttg | agt | cta | gct | tta | cca | gat | gat | gac | gga | agt | gat | gag | 1170 |
| Ala | Ala | Asn | Leu | Ser | Leu | Ala | Leu | Pro | Asp | Asp | Asp | Gly | Ser | Asp | Glu |      |
|     |     |     |     | 345 |     |     |     |     | 350 |     |     |     |     | 355 |     |      |
| agc | agt | cca | cca | tca | gcc | tcc | cct | gct | gaa | tct | gag | cca | cag | tgt | gat | 1218 |
| Ser | Ser | Pro | Pro | Ser | Ala | Ser | Pro | Ala | Ğlu | Ser | Glu | Pro | Gln | Cys | Asp |      |

|             | 360         |            | 365           | 370                   |      |
|-------------|-------------|------------|---------------|-----------------------|------|
|             |             |            |               |                       |      |
|             |             |            |               | gca ttg cta gaa gcc   | 1266 |
| Pro Ser Phe | Lys Gly A   | sp Ala Gly | Glu Asn Thr   | Ala Leu Leu Glu Ala   |      |
| 375         | j           | 380        |               | 385                   |      |
| ggc agg agt | gac tot ca  | gg cat gga | gga ccc atc   | tcc tagcacac          | 1310 |
| Gly Arg Ser | Asp Ser A   | rg His Gly | Gly Pro Ile   | Ser                   |      |
| 390         |             | 395        |               | 400                   |      |
| gtgcccactg  | aagtggcacc  | aacagaagti | t tggcttgaac  | taaaggacat tttattttt  | 1370 |
| ttactttagc  | acataatttg  | tatatttgaa | a aataatgtat  | attattttac ctattagatt | 1430 |
| ctgatttgat  | atacaaagga  | ctaagatati | t ttcttcttga  | agagactttt cgattagtcc | 1490 |
| tcatatattt  | atctactaaa  | atagagtgti | t taccatg     |                       | 1527 |
|             |             |            |               |                       |      |
| <210> 119   |             |            |               |                       |      |
| <211> 1905  |             |            |               |                       |      |
| <212> DNA   |             |            |               |                       |      |
| <213> Homo  | sapiens     |            |               |                       |      |
| <220>       |             |            |               |                       |      |
| <221> CDS   |             |            |               |                       |      |
| <222> (125) | (703)       |            |               |                       |      |
| <400> 119   |             |            |               |                       |      |
| gagcctaacc  | tagagtgctc  | gcagcagtct | ttcagttgag    | cttggggact gcagctgtgg | 60   |
| ggagatttca  | gtgcattgcc  | tcccctgggt | gctcttcatc    | ttggatttga aagttgagag | 120  |
| cagc atg tt | t tgc cca c | tg aaa cto | atc ctg ct    | g cca gtg tta ctg gat | 169  |
| Met Ph      | e Cys Pro L | eu Lys Lei | ı Ile Leu Leı | u Pro Val Leu Leu Asp |      |
|             |             |            | .~            |                       |      |

5

l

| tat | tcc | ttg | ggc | ctg | aat | gac | ttg | aat | gtt | tcc | ccg | cct | gag        | cta | aca | 217 |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|------------|-----|-----|-----|
| Tyr | Ser | Leu | Gly | Leu | Asn | Asp | Leu | Asn | Val | Ser | Pro | Pro | Glu        | Leu | Thr |     |
|     |     |     |     | 20  |     |     |     |     | 25  |     |     |     |            | 30  |     |     |
| gtc | cat | gtg | ggt | gat | tca | gct | ctg | atg | gga | tgt | gtt | ttc | cag        | agc | aca | 265 |
| Val | His | Val | Gly | Asp | Ser | Ala | Leu | Met | Gly | Cys | Val | Phe | Gln        | Ser | Thr |     |
|     |     |     | 35  |     |     |     |     | 40  |     |     |     |     | <b>4</b> 5 |     |     |     |
| gaa | gac | aaa | tgt | ata | ttc | aag | ata | gac | tgg | act | ctg | tca | cca        | gga | gag | 313 |
| Glu | Asp | Lys | Cys | Ile | Phe | Lys | Ile | Asp | Trp | Thr | Leu | Ser | Pro        | Gly | Glu |     |
|     |     | 50  |     |     |     |     | 55  |     |     |     |     | 60  |            |     |     |     |
| cac | gcc | aag | gac | gaa | tat | gtg | cta | tac | tat | tac | tcc | aat | ctc        | agt | gtg | 361 |
| His | Ala | Lys | Asp | Glu | Tyr | Val | Leu | Tyr | Tyr | Tyr | Ser | Asn | Leu        | Ser | Val |     |
|     | 65  |     |     |     |     | 70  |     |     |     |     | 75  |     |            |     |     |     |
| cct | att | ggg | cgc | ttc | cag | aac | cgc | gta | cac | ttg | atg | ggg | gac        | aac | tta | 409 |
| Pro | lle | Gly | Arg | Phe | Gln | Asn | Arg | Val | His | Leu | Met | Gly | Asp        | Asn | Leu |     |
| 80  |     |     |     |     | 85  |     |     |     |     | 90  |     |     |            |     | 95  |     |
| tgc | aat | gat | ggc | tct | ctc | ctg | ctc | caa | gat | gtg | caa | gag | gct        | gac | cag | 457 |
| Cys | Asn | Asp | Gly | Ser | Leu | Leu | Leu | Gln | Asp | Val | Gln | Glu | Ala        | Asp | Gln |     |
|     |     |     |     | 100 |     |     |     |     | 105 |     |     |     |            | 110 |     |     |
| gga | acc | tat | atc | tgt | gaa | atc | cgc | ctc | aaa | ggg | gag | agc | cag        | gtg | ttc | 505 |
| Gly | Thr | Tyr | Ile | Cys | Glu | Ile | Arg | Leu | Lys | Gly | Glu | Ser | Gln        | Val | Phe |     |
|     |     |     | 115 |     |     |     |     | 120 |     |     |     |     | 125        |     |     |     |
| aag | aag | gcg | gtg | gta | ctg | cat | gtg | ctt | cca | gag | gag | ccc | aaa        | gag | ctc | 553 |
| Lys | Lys | Ala | Val | Val | Leu | His | Val | Leu | Pro | Glu | Glu | Pro | Lys        | Glu | Leu |     |
|     |     | 130 |     |     |     |     | 135 |     | ند. |     |     | 140 |            |     |     |     |
| atg | gtc | cat | gtg | ggt | gga | ttg | att | cag | atg | gga | tgt | gtt | ttc        | cag | agc | 601 |

| Met Val His V | /al Gly Gly Leu Ile  | Gln Met Gly ( | Cys Val Phe Gln Ser    |      |
|---------------|----------------------|---------------|------------------------|------|
| 145           | 150                  |               | 155                    |      |
| aca gaa gtg a | aaa cac gtg acc aag  | gta gaa tgg   | ata ttt tca gga cgg    | 649  |
| Thr Glu Val L | ys His Val Thr Lys   | Val Glu Trp   | Ile Phe Ser Gly Arg    |      |
| 160           | 165                  | 170           | 175                    |      |
| cgc gca aag g | gta aca agg agg aaa  | cat cac tgt   | gtt aga gaa ggc tct    | 697  |
| Arg Ala Lys V | /al Thr Arg Arg Lys  | His His Cys ' | Val Arg Glu Gly Ser    |      |
|               | 180                  | 185           | 190                    |      |
| ggc tgatggtat | c aggacaaagg tagaat  | cagg cacatga  | gga ggtgttgcaa         | 750  |
| Gly           |                      |               |                        |      |
| gagcctgggc tt | tggtgctt atcagaactg  | gaccttctcc    | tagcaatttc agctttctgg  | 810  |
| tgggaaagat aa | nctccaatg aagaacaaga | acaagaagat    | gatgatgatg cttaactttt  | 870  |
| tggatgccga ta | itgagattg tacatgagga | gattgtattt d  | cgttactacc acaaactcag  | 930  |
| gatgtctgcg ga | igtactccc agagctgggg | ccacttccag a  | aatcgtgtga acctggtggg  | 990  |
| ggacattttc cg | caatgacg gttccatcat  | gcttcaagga (  | gtgagggagt cagatggagg  | 1050 |
| aaactacacc tg | gcagtatcc acctagggaa | cctggtgttc    | aagaaaacca ttgtgctgca  | 1110 |
| tgtcagcccg ga | agageete gaacaetggt  | gaccccggca    | gccctgaggc ctctggtctt  | 1170 |
| gggtggtaat ca | gttggtga tcattgtggg  | aattgtctgt g  | gccacaatcc tgctgctccc  | 1230 |
| tgttctgata tt | gatcgtga agaagacctg  | tggaaataag a  | agttcagtga attctacagt  | 1290 |
| cttggtgaag aa | cacgaaga agactaatcc  | agagataaaa g  | gaaaaaaccct gccattttga | 1350 |
| aagatgtgaa gg | ggagaaac acatttactc  | cccaataatt g  | gtacgggagg tgatcgagga  | 1410 |
| agaagaacca ag | tgaaaaat cagaggccac  | ctacatgacc a  | atgcacccag tttggccttc  | 1470 |
| tctgaggtca ga | tcggaaca actcacttga  | aaaaaagtca g  | ggtgggggaa tgccaaaaac  | 1530 |
| acagcaagcc tt | ttgagaag aatggagagt  | cccttcatct o  | cagcagcggt ggagactctc  | 1590 |
| tcctgtgtgt gt | cctgggcc actctaccag  | tgatttcaga o  | ctcccgctct cccagctgtc  | 1650 |

| ctcctgtctc attgtttggt caatacac | tg aagatggaga  | atttggagcc tggcagaga  | ag 1710 |
|--------------------------------|----------------|-----------------------|---------|
| actggacagc tctggaggaa caggcctg | ct gaggggaggg  | gagcatggac ttggcctc   | tg 1770 |
| gagtgggaca ctggccctgg gaaccagg | ct gagctgagtg  | gecteaaacc ccccgttgg  | ga 1830 |
| tcagaccete ctgtgggcag ggttctta | gt ggatgagtta  | ctgggaagaa tcagagata  | aa 1890 |
| aaaccaaccc aaatc               |                |                       | 1905    |
|                                |                |                       |         |
| <210> 120                      |                |                       |         |
| <211> 998                      |                |                       |         |
| <212> DNA                      |                |                       |         |
| <213> Homo sapiens             |                |                       |         |
| <220>                          |                |                       |         |
| <221> CDS                      |                |                       |         |
| <222> (50)(832)                |                |                       |         |
| <400> 120                      |                |                       |         |
| gcacttgcca gccagtccgc ccgtccgg | ag cccggctcg   | tggggcagc atg gcg     | 55      |
|                                |                | Met Ala               |         |
|                                |                | 1                     |         |
| ggg tcg ccg ctg ctc tgg ggg cc | g cgg gcc ggg  | g ggc gtc ggc ctt ttg | 103     |
| Gly Ser Pro Leu Leu Trp Gly Pr | o Arg Ala Gly  | / Gly Val Gly Leu Leu |         |
| 5                              | 0              | 15                    |         |
| gtg ctg ctg ctc ctc ggc ctg tt | t cgg ccg cc   | c ccc gcg ctc tgc gcg | 151     |
| Val Leu Leu Leu Gly Leu Pr     | e Arg Pro Pro  | o Pro Ala Leu Cys Ala |         |
| 20 25                          |                | 30                    |         |
| cgg ccg gta aag gag ccc cgc gg | go ota ago goa | a gog tot oog ooc ttg | 199     |

Arg Pro Val Lys Glu Pro Arg Gly Leú Ser Ala Ala Ser Pro Pro Leu

| 35  |     |     |     |     | 40  |     |     |     |     | 45   |     |     |     |     | 50  |     |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|------|-----|-----|-----|-----|-----|-----|
| gct | gag | act | ggc | gct | cct | cgc | cgc | ttc | cgg | cgg  | tca | gtg | ccc | cga | ggt | 247 |
| Ala | Glu | Thr | Gly | Ala | Pro | Arg | Arg | Phe | Arg | Arg  | Ser | Val | Pro | Arg | Gly |     |
|     |     |     |     | 55  |     |     |     |     | 60  |      |     |     |     | 65  |     |     |
| gag | gcg | gcg | ggg | gcg | gtg | cag | gag | ctg | gcg | cgg  | gcg | ctg | gcg | cat | ctg | 295 |
| Glu | Ala | Ala | Gly | Ala | Val | Gln | Glu | Leu | Ala | Arg  | Ala | Leu | Ala | His | Leu |     |
|     |     |     | 70  |     |     |     |     | 75  |     |      |     |     | 80  |     |     |     |
| ctg | gag | gcc | gaa | cgt | cag | gag | cgg | gcg | cgg | gcc  | gag | gcg | cag | gag | gct | 343 |
| Leu | Glu | Ala | Glu | Arg | Gln | Glu | Arg | Ala | Arg | Ala  | Glu | Ala | G1n | Glu | Ala |     |
|     |     | 85  |     |     |     |     | 90  |     |     |      |     | 95  |     |     |     |     |
| gag | gat | cag | cag | gcg | cgc | gtc | ctg | gcg | cag | ctg  | ctg | cgc | gtc | tgg | ggc | 391 |
| Glu | Asp | Gln | Gln | Ala | Arg | Val | Leu | Ala | Gln | Leu  | Leu | Arg | Val | Trp | Gly |     |
|     | 100 |     |     |     |     | 105 |     |     |     |      | 110 |     |     |     |     |     |
| gcc | ccc | cgc | aac | tct | gat | ccg | gct | ctg | ggc | ctg. | gac | gac | gac | ccc | gac | 439 |
| Ala | Pro | Arg | Asn | Ser | Asp | Pro | Ala | Leu | Gly | Leu  | Asp | Asp | Asp | Pro | Asp |     |
| 115 |     |     |     |     | 120 |     |     |     |     | 125  |     |     |     |     | 130 |     |
| gcg | cct | gca | gcg | cag | ctc | gct | cgc | gct | ctg | ctc  | cgc | gcc | cgc | ctt | gac | 487 |
| Ala | Pro | Ala | Ala | Gln | Leu | Ala | Arg | Ala | Leu | Leu  | Arg | Ala | Arg | Leu | Asp |     |
|     |     |     |     | 135 |     |     |     |     | 140 |      |     |     |     | 145 |     |     |
| cct | gcc | gcc | ctc | gca | gcc | cag | ctt | gtc | ccc | gcg  | ccc | gtc | ccc | gcc | gcg | 535 |
| Pro | Ala | Ala | Leu | Ala | Ala | Gln | Leu | Val | Pro | Ala  | Pro | Val | Pro | Ala | Ala |     |
|     |     |     | 150 |     |     |     |     | 155 |     |      |     |     | 160 |     |     |     |
| gcg | ctc | cga | ccc | cgg | ccc | ccg | gtc | tac | gac | gac  | ggc | ccc | gcg | ggc | ccg | 583 |
| Ala | Leu | Arg | Pro | Arg | Pro | Pro | Val | Tyr | Asp | Asp  | Gly | Pro | Ala | Gly | Pro |     |
|     |     | 165 |     |     |     |     | 170 |     |     |      |     | 175 |     |     |     | •   |

| gat  | gct   | gag   | gag   | gca   | ggc   | gac   | gag   | aca   | ссс   | gac   | gtg  | gac   | ccc   | gag   | ctg    | 631 |
|------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|------|-------|-------|-------|--------|-----|
| Asp  | Ala   | Glu   | Glu   | Ala   | Gly   | Asp   | Glu   | Thr   | Pro   | Asp   | Val  | Asp   | Pro   | Glu   | Leu    |     |
|      | 180   |       |       |       |       | 185   |       |       |       |       | 190  |       |       |       |        |     |
| ttg  | agg   | tac   | ttg   | ctg   | gga   | cgg   | att   | ctt   | gcg   | gga   | agc  | gcg   | gac   | tcc   | gag    | 679 |
| Leu  | Arg   | Tyr   | Leu   | Leu   | Gly   | Arg   | Ile   | Leu   | Ala   | Gly   | Ser  | Ala   | Asp   | Ser   | Glu    |     |
| 195  |       |       |       |       | 200   |       |       |       |       | 205   |      |       |       |       | 210    |     |
| ggg  | gtg   | gca   | gcc   | ccg   | cgc   | cgc   | ctc   | cgc   | cgt   | gcc   | gcc  | gac   | cac   | gat   | gtg    | 727 |
| Gly  | Val   | Ala   | Ala   | Pro   | Arg   | Arg   | Leu   | Arg   | Arg   | Ala   | Ala  | Asp   | His   | Asp   | Val    |     |
|      |       |       |       | 215   |       |       |       |       | 220   |       |      |       |       | 225   |        |     |
| ggc  | tct   | gag   | ctg   | ccc   | cct   | gag   | ggc   | gtg   | ctg   | ggg   | gcg  | ctg   | ctg   | cgt   | gtg    | 775 |
| Gly  | Ser   | Glu   | Leu   | Pro   | Pro   | Glu   | Gly   | Val   | Leu   | Gly   | Ala  | Leu   | Leu   | Arg   | Val    |     |
|      |       |       | 230   |       |       |       |       | 235   |       |       |      |       | 240   |       |        |     |
| aaa  | cgc   | cta   | gag   | acc   | ccg   | gcg   | ccc   | cag   | gtg   | cct   | gca  | cgc   | cgc   | ctc   | ttg    | 823 |
| Lys  | Arg   | Leu   | Glu   | Thr   | Pro   | Ala   | Pro   | Gln   | Val   | Pro   | Ala  | Arg   | Arg   | Leu   | Leu    |     |
|      |       | 245   |       |       |       |       | 250   |       |       |       |      | 255   |       |       |        |     |
| cca  | ccc   | t ga  | agcad | etgeo | c cgg | gatco | ecgt  | gcad  | eccte | ggg a | ссса | agaag | gt go | cccc  | egeca  | 880 |
| Pro  | Pro   |       |       |       |       |       |       |       |       |       |      |       |       |       |        |     |
|      | 260   |       |       |       |       |       |       |       |       |       |      |       |       |       |        |     |
| tccc | egcca | acc a | aggao | etget | tc co | ecge  | cagca | a cgi | ccae  | gagc  | aact | taco  | cc g  | ggcca | agccag | 940 |
| ccct | ctca  | acc ( | cgagg | gated | ee ta | ccc   | ectg  | g cco | caca  | ata   | aaca | atga  | tct g | gaago | cagc   | 998 |

<210> 121

<211> 337

<212> PRT

<213> Homo sapiens

| <400> 121 |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |
|-----------|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
| Met       | Thr | Ala | Gly | Gly | G1n | Ala | Glu | Ala | Glu | Gly | Ąla | Gly | Gly | Glu | Pro |
| 1         |     |     |     | 5   |     |     |     |     | 10  |     |     |     |     | 15  |     |
| Gly       | Ala | Ala | Arg | Leu | Pro | Ser | Arg | Val | Ala | Arg | Leu | Leu | Ser | Ala | Leu |
|           |     |     | 20  |     |     |     |     | 25  |     |     |     |     | 30  |     | •   |
| Phe       | Tyr | Gly | Thr | Cys | Ser | Phe | Leu | Ile | Val | Leu | Val | Asn | Lys | Ala | Leu |
|           |     | 35  |     |     |     |     | 40  |     |     |     |     | 45  |     |     |     |
| Leu       | Thr | Thr | Tyr | Gly | Phe | Pro | Ser | Pro | Ile | Phe | Leu | Gly | Ile | Gly | Gln |
|           | 50  |     |     |     |     | 55  |     |     |     |     | 60  |     |     |     |     |
| Met       | Ala | Ala | Thr | Ile | Met | Ile | Leu | Tyr | Val | Ser | Lys | Leu | Asn | Lys | Ile |
| 65        |     |     |     |     | 70  |     |     |     |     | 75  |     |     |     |     | 80  |
| Ile       | His | Phe | Pro | Asp | Phe | Asp | Lys | Lys | Ile | Pro | Val | Lys | Leu | Phe | Pro |
|           |     |     |     | 85  |     |     |     |     | 90  |     |     |     |     | 95  |     |
| Leu       | Pro | Leu | Leu | Tyr | Val | Gly | Asn | His | Ile | Ser | Gly | Leu | Ser | Ser | Thr |
|           |     |     | 100 |     |     |     |     | 105 |     |     |     |     | 110 |     |     |
| Ser       | Lys | Leu | Ser | Leu | Pro | Met | Phe | Thr | Val | Leu | Arg | Lys | Phe | Thr | Ile |
|           |     | 115 |     |     |     |     | 120 |     |     |     |     | 125 |     |     |     |
| Pro       | Leu | Thr | Leu | Leu | Leu | Glu | Thr | Ile | Ile | Leu | Gly | Lys | Gln | Tyr | Ser |
|           | 130 |     |     |     |     | 135 |     |     |     |     | 140 |     |     |     |     |
| Leu       | Asn | He  | Ile | Leu | Ser | Val | Phe | Ala | Ile | Ile | Leu | Gly | Ala | Phe | Ile |
| 145       |     |     |     |     | 150 |     |     |     |     | 155 |     |     |     |     | 160 |
| Ala       | Ala | Gly | Ser | Asp | Leu | Ala | Phe | Asn | Leu | Glu | Gly | Tyr | Ile | Phe | Val |
|           |     |     |     | 165 |     |     |     |     | 170 |     |     |     |     | 175 |     |
| Phe       | Leu | Asn | Asp | He  | Phe | Thr | Ala | ۸la | Asn | Gly | Val | Tyr | Thr | Lvs | Gln |

190

180

| Lys | Met                                 | Asp   | Pro   | Lys | Glu | Leu   | Gly  | Lys | Tyr | Gly | Val | Leu | Phe | Tyr | Asr   |
|-----|-------------------------------------|---|---|-----|-----|---|--|-----|-----|-----|-----|-----|-----|-----|---|
|     |                                     | 195   |   |     |     |   | 200  |     |     |     |     | 205 |     |     |   |
| Ala | Cys                                 | Phe   | Met   | Ile | Ile | Pro   | Thr  | Leu | Ile | Ile | Ser | Val | Ser | Thr | Gly   |
|     | 210                                 |   |   |     |     | 215   |  |     |     |     | 220 |     |     |     |   |
| Asp | Leu                                 | Gln   | Gln   | Ala | Thr | Glu   | Phe  | Asn | G1n | Trp | Lys | Asn | Val | Val | Phe   |
| 225 |                                     |   |   |     | 230 |   |  |     |     | 235 |     |     |     |     | 240   |
| Ile | Leu                                 | Gln   | Phe   | Leu | Leu | Ser   | Cys  | Phe | Leu | Gly | Phe | Leu | Leu | Met | Tyr   |
|     |                                     |   |   | 245 |     |   |  |     | 250 |     |     |     |     | 255 |   |
| Ser | Thr                                 | Val   | Leu   | Cys | Ser | Tyr   | Tyr  | Asn | Ser | Ala | Leu | Thr | Thr | Ala | Val   |
|     |                                     |   | 260   |     |     |   |  | 265 |     |     |     |     | 270 |     |   |
| Val | Gly                                 | Ala   | Ile   | Lys | Asn | Val   | Ser  | Val | Ala | Tyr | Ile | Gly | Ile | Leu | Πe  |
|     |                                     | 275   |   |     |     |   | 280  |     |     |     |     | 285 |     |     |   |
| Gly | Gly                                 | Asp   | Tyr   | He  | Phe | Ser   | Leu  | Leu | Asn | Phe | Val | Gly | Leu | Asn | Πe  |
|     | 290                                 |   |   |     |     | 295   |  |     |     |     | 300 |     |     |     |   |
| Cys | Met                                 | Ala   | Gly   | Gly | Leu | Arg   | Tyr  | Ser | Phe | Leu | Thr | Leu | Ser | Ser | Gln   |
| 305 |                                     |   |   |     | 310 |   |  |     |     | 315 |     |     |     |     | 320   |
| Leu | Lys                                 | Pro   | Lys   | Pro | Val | Gly   | Glu  | Glu | Asn | Ile | Cys | Leu | Asp | Leu | Lys   |
|     |                                     |   |   | 325 |     |   |  |     | 330 |     |     |     |     | 335 |   |
|     | Ala Asp 225 Ile Ser Val Gly Cys 305 | Ala Cys 210 Asp Leu 225 Ile Leu Ser Thr Val Gly Gly Gly 290 Cys Met 305 | 195 Ala Cys Phe 210  Asp Leu Gln 225 Ile Leu Gln  Ser Thr Val  Val Gly Ala 275 Gly Gly Asp 290  Cys Met Ala 305 | 195 | 195 | 195         195         Ala       Cys       Phe       Met       Ile       Ile         210 | 195         Ala       Cys       Phe       Met       Ile       Ile       Pro         210       June       June       215         Asp       Leu       Gln       Ala       Thr       Glu         225       June       June       230       June       June< | 195 | 195 | 195 | 195 | 195 | 195 | 195 | Ala Cys Phe Met IIe IIe Pro Thr Leu IIe IIe Ser Val Ser Thr 210 |

<210> 122

Ser

<211> 236

<212> PRT

<213> Homo sapiens

| <40 | 0> 1 | 22  |     |     |     |     |     |     |     |     |     |     |     |     |     |
|-----|------|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
| Met | Ala  | Glu | Ala | Glu | Glu | Ser | Pro | G1y | Asp | Pro | Gly | Thr | Ala | Ser | Pro |
| 1   |      |     |     | 5   |     |     |     |     | 10  |     |     |     |     | 15  |     |
| Arg | Pro  | Leu | Phe | Ala | Gly | Leu | Ser | Asp | Ile | Ser | Ile | Ser | G1n | Asp | Ile |
|     |      |     | 20  |     |     |     |     | 25  |     |     |     |     | 30  |     |     |
| Pro | Val  | Glu | Gly | Glu | Ile | Thr | Ile | Pro | Met | Arg | Ser | Arg | Ile | Arg | Glu |
|     |      | 35  |     |     |     |     | 40  |     |     |     |     | 45  |     |     |     |
| Phe | Asp  | Ser | Ser | Thr | Leu | Asn | Glu | Ser | Val | Arg | Asn | Thr | Ile | Met | Arg |
|     | 50   |     |     |     |     | 55  |     |     |     |     | 60  |     |     |     |     |
| Asp | Leu  | Lys | Ala | Val | Gly | Lys | Lys | Phe | Met | His | Val | Leu | Tyr | Pro | Arg |
| 65  |      |     |     |     | 70  |     |     |     |     | 75  |     |     |     |     | 80  |
| Lys | Ser  | Asn | Thr | Leu | Leu | Arg | Asp | Trp | Asp | Leu | Trp | Gly | Pro | Leu | Ile |
|     |      |     |     | 85  |     |     |     |     | 90  |     |     |     |     | 95  |     |
| Leu | Cys  | Val | Thr | Leu | Ala | Leu | Met | Leu | Gln | Arg | Asp | Ser | Ala | Asp | Ser |
|     |      |     | 100 |     |     |     |     | 105 |     |     |     |     | 110 |     |     |
| Glu | Lys  | Asp | Gly | Gly | Pro | Gln | Phe | Ala | Glu | Val | Phe | Val | Ile | Val | Trp |
|     |      | 115 |     |     |     |     | 120 |     |     |     |     | 125 |     |     |     |
| Phe | Gly  | Ala | Val | Thr | Ile | Thr | Leu | Asn | Ser | Lys | Leu | Leu | Gly | Gly | Asn |
|     | 130  |     |     |     |     | 135 |     |     |     |     | 140 |     |     |     |     |
| He  | Ser  | Phe | Phe | Gln | Ser | Leu | Cys | Val | Leu | Gly | Tyr | Cys | Ile | Leu | Pro |
| 145 |      |     |     |     | 150 |     |     |     |     | 155 |     |     |     |     | 160 |
| Leu | Thr  | Val | Ala | Met | Leu | Ile | Cys | Arg | Leu | Val | Leu | Leu | Ala | Asp | Pro |
|     |      |     |     | 165 |     |     |     |     | 170 |     |     |     |     | 175 |     |
| Gly | Pro  | Val | Asn | Phe | Met | Val | Arg | Leu | Phe | Val | Val | Ile | Val | Met | Phe |

185

190

180

WO 01/12660

#### 256/307

Ala Trp Ser Ile Val Ala Ser Thr Ala Phe Leu Ala Asp Ser Gln Pro 195 200 205 Pro Asn Arg Arg Ala Leu Ala Val Tyr Pro Val Phe Leu Phe Tyr Phe 210 215 220 Val Ile Ser Trp Met Ile Leu Thr Phe Thr Pro Gln 225 230 235 <210> 123 <211> 560 <212> PRT <213> Homo sapiens <400> 123 Met Ala Ala Pro Ala Glu Ser Leu Arg Arg Arg Lys Thr Gly Tyr Ser l 5 10 15 Asp Pro Glu Pro Glu Ser Pro Pro Ala Pro Gly Arg Gly Pro Ala Gly 20 25 30 Ser Pro Ala His Leu His Thr Gly Thr Phe Trp Leu Thr Arg Ile Val 35 40 45 Leu Leu Lys Ala Leu Ala Phe Val Tyr Phe Val Ala Phe Leu Val Ala 50 55 Phe His Gln Asn Lys Gln Leu Ile Gly Asp Arg Gly Leu Leu Pro Cys 65 70 75 80 Arg Val Phe Leu Lys Asn Phe Gln Gln Tyr Phe Gln Asp Arg Thr Ser 85 90 95 Trp Glu Val Phe Ser Tyr Met Pro Thr Ile Leu Trp Leu Met Asp Trp

|     |     |     | 100 |     |     |     |     | 105 |     |     |     |     | 110 |     |     |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
| Ser | Asp | Met | Asn | Ser | Asn | Leu | Asp | Leu | Leu | Ala | Leu | Leu | Gly | Leu | Gly |
|     |     | 115 |     |     |     |     | 120 |     |     |     |     | 125 |     |     |     |
| Ile | Ser | Ser | Phe | Val | Leu | Ile | Thr | Gly | Cys | Ala | Asn | Met | Leu | Leu | Met |
|     | 130 |     |     |     |     | 135 |     |     |     |     | 140 |     |     |     |     |
| Ala | Ala | Leu | Trp | Gly | Leu | Tyr | Met | Ser | Leu | Val | Asn | Val | Gly | His | Val |
| 145 |     |     |     |     | 150 |     |     |     |     | 155 |     |     |     |     | 160 |
| Trp | Tyr | Ser | Phe | Gly | Trp | Glu | Ser | Gln | Leu | Leu | Glu | Thr | Gly | Phe | Leu |
|     |     |     |     | 165 |     |     |     |     | 170 |     |     |     |     | 175 |     |
| Gly | Ile | Phe | Leu | Cys | Pro | Leu | Trp | Thr | Leu | Ser | Arg | Leu | Pro | Gln | His |
|     |     |     | 180 |     |     |     |     | 185 |     |     |     |     | 190 |     |     |
| Thr | Pro | Thr | Ser | Λrg | Ile | Val | Leu | Trp | Gly | Phe | Arg | Trp | Leu | Ile | Phe |
|     |     | 195 |     |     |     |     | 200 |     |     |     |     | 205 |     |     |     |
| Arg | Ile | Met | Leu | Gly | Ala | Gly | Leu | Ile | Lys | He  | Arg | Gly | Λsp | Arg | Cys |
|     | 210 |     |     |     |     | 215 |     |     |     |     | 220 |     |     |     |     |
| Trp | Arg | Asp | Leu | Thr | Cys | Met | Asp | Phe | His | Tyr | Glu | Thr | Gln | Pro | Met |
| 225 |     |     |     |     | 230 |     |     |     |     | 235 |     |     |     |     | 240 |
| Pro | Asn | Pro | Val | Ala | Tyr | Tyr | Leu | His | His | Ser | Pro | Trp | Trp | Phe | His |
|     |     |     |     | 245 |     |     |     |     | 250 |     |     |     |     | 255 |     |
| Arg | Phe | Glu | Thr | Leu | Ser | Asn | His | Phe | Ile | Glu | Leu | Leu | Val | Pro | Phe |
|     |     |     | 260 |     |     |     |     | 265 |     |     |     |     | 270 |     |     |
| Phe | Leu | Phe | Leu | Gly | Arg | Arg | Ala | Cys | Ile | Ile | His | Gly | Val | Leu | Gln |
|     |     | 275 |     |     |     |     | 280 |     |     |     |     | 285 |     |     |     |
| Ile | Leu | Phe | Gln | Ala | Val | Leu | Ile | Val | Ser | Gly | Asn | Leu | Ser | Phe | Leu |
|     | 290 |     |     |     |     | 295 |     | /   |     |     | 300 |     |     |     |     |

| Asn | Trp | Leu | Thr | Met | Val | Pro | Ser | Leu  | Ala | Cys | Phe | Asp | Asp | Ala | Thr |
|-----|-----|-----|-----|-----|-----|-----|-----|------|-----|-----|-----|-----|-----|-----|-----|
| 305 |     |     |     |     | 310 |     |     |      |     | 315 |     |     |     |     | 320 |
| Leu | Gly | Phe | Leu | Phe | Pro | Ser | Gly | Pro  | Gly | Ser | Leu | Lys | Asp | Arg | Val |
|     |     |     |     | 325 |     |     | ٠   |      | 330 |     |     |     |     | 335 |     |
| Leu | Gln | Met | Gln | Arg | Asp | Ile | Arg | Gly  | Ala | Arg | Pro | Glu | Pro | Arg | Phe |
|     |     |     | 340 |     |     |     |     | 345  |     |     |     |     | 350 |     |     |
| Gly | Ser | Val | Val | Arg | Arg | Ala | Ala | Asn  | Val | Ser | Leu | Gly | Val | Leu | Leu |
|     |     | 355 |     |     |     |     | 360 |      |     |     |     | 365 |     |     |     |
| Ala | Trp | Leu | Ser | Val | Pro | Val | Val | Leu  | Åsn | Leu | Leu | Ser | Ser | Arg | Gln |
|     | 370 |     |     |     |     | 375 |     |      |     |     | 380 |     |     |     |     |
| Val | Met | Asn | Thr | His | Phe | Asn | Ser | Leu  | His | Ile | Val | Asn | Thr | Tyr | Gly |
| 385 |     |     |     |     | 390 |     |     |      |     | 395 |     |     |     |     | 400 |
| Ala | Phe | Gly | Ser | He  | Thr | Lys | Glu | Arg  | Ala | Glu | Val | He  | Leu | Gln | Gly |
|     |     |     |     | 405 |     |     |     |      | 410 |     |     |     |     | 415 |     |
| Thr | Ala | Ser | Ser | Asn | Ala | Ser | Ala | Pro  | Asp | Ala | Met | Trp | Glu | Asp | Tyr |
|     |     |     | 420 |     |     |     |     | 425  |     |     |     |     | 430 |     |     |
| Glu | Phe | Lys | Cys | Lys | Pro | Gly | Asp | Pro  | Ser | Arg | Arg | Pro | Cys | Leu | Ile |
|     |     | 435 |     |     |     |     | 440 |      |     |     |     | 445 |     |     |     |
| Ser | Pro | Tyr | His | Tyr | Arg | Leu | Asp | Trp  | Leu | Met | Trp | Phe | Ala | Ala | Phe |
|     | 450 |     |     |     |     | 455 |     |      |     |     | 460 |     |     |     |     |
| Gln | Thr | Tyr | Glu | His | Asn | Asp | Trp | Ile  | Ile | His | Leu | Ala | Gly | Lys | Leu |
| 465 |     |     |     |     | 470 |     |     |      |     | 475 |     |     |     |     | 480 |
| Leu | Ala | Ser | Asp | Ala | Glu | Ala | Leu | Ser  | Leu | Leu | Ala | His | Asn | Pro | Phe |
|     |     |     |     | 485 |     |     |     |      | 490 |     |     |     |     | 495 |     |
| Ala | Gly | Arg | Pro | Pro | Pro | Arg | Trp | Val- | Arg | Glv | Glu | His | Tvr | Arg | Tvr |

Lys Phe Ser Arg Pro Gly Gly Arg His Ala Ala Glu Gly Lys Trp Trp Val Arg Lys Arg Ile Gly Ala Tyr Phe Pro Pro Leu Ser Leu Glu Glu Leu Arg Pro Tyr Phe Arg Asp Arg Gly Trp Pro Leu Pro Gly Pro Leu <210> 124 <211> 406 <212> PRT <213> Homo sapiens <400> 124 Met Ala Glu Asn Gly Lys Asn Cys Asp Gln Arg Arg Val Ala Met Asn Lys Glu His His Asn Gly Asn Phe Thr Asp Pro Ser Ser Val Asn Glu Lys Lys Arg Arg Glu Arg Glu Arg Gln Asn Ile Val Leu Trp Arg Gln Pro Leu Ile Thr Leu Gln Tyr Phe Ser Leu Glu Ile Leu Val Ile Leu Lys Glu Trp Thr Ser Lys Leu Trp His Arg Gln Ser Ile Val Val Ser Phe Leu Leu Leu Ala Val Leu Ile Ala Thr Tyr Tyr Val Glu

| Gly | Val | His   | Gln | Gln | Tyr   | Val | Gln | Arg | Ile     | Glu | Lys | Gln | Phe | Leu | Leu |
|-----|-----|-------|-----|-----|-------|-----|-----|-----|---------|-----|-----|-----|-----|-----|-----|
|     |     |       | 100 |     |       |     |     | 105 |         |     |     |     | 110 |     |     |
| Tyr | Ala | Tyr   | Trp | Ile | Gly   | Leu | Gly | He  | Leu     | Ser | Ser | Val | Gly | Leu | Gly |
|     |     | 115   |     |     |       |     | 120 |     |         |     |     | 125 |     |     |     |
| Thr | Gly | Leu   | His | Thr | Phe   | Leu | Leu | Tyr | Leu     | Gly | Pro | His | Ile | Ala | Ser |
|     | 130 |       |     |     |       | 135 |     |     |         |     | 140 |     |     |     |     |
| Val | Thr | Leu   | Ala | Ala | Tyr   | Glu | Cys | Asn | Ser     | Val | Asn | Phe | Pro | Glu | Pro |
| 145 |     |       |     |     | 150   |     |     |     |         | 155 |     |     |     |     | 160 |
| Pro | Tyr | Pro   | Asp | Gln | Ile   | Ile | Cys | Pro | Asp     | Glu | Glu | Gly | Thr | Glu | Gly |
|     |     |       |     | 165 |       |     |     |     | 170     |     |     |     |     | 175 |     |
| Thr | Ile | Ser   | Leu | Trp | Ser   | Ile | Ile | Ser | Lys     | Val | Arg | Ile | Glu | Ala | Cys |
|     |     |       | 180 |     |       |     |     | 185 |         |     |     |     | 190 |     |     |
| Met | Trp | Gly   | Ile | Gly | Thr   | Ala | Ile | Gly | Glu     | Leu | Pro | Pro | Tyr | Phe | Met |
|     |     | 195   |     |     |       |     | 200 |     |         |     |     | 205 |     |     |     |
| Ala | Arg | Ala   | Λla | Arg | Leu   | Ser | Gly | Ala | Glu     | Pro | Asp | Asp | Glu | Glu | Tyr |
|     | 210 |       |     |     |       | 215 |     |     |         |     | 220 |     |     |     |     |
| Gln | Glu | Phe   | Glu | Glu | Met   | Leu | Glu | His | Ala     | Glu | Ser | Ala | Gln | Asp | Phe |
| 225 |     |       |     |     | 230   |     |     |     |         | 235 |     |     |     |     | 240 |
| Ala | Ser | Arg   | Ala | Lys | Leu   | Ala | Val | Gln | Lys     | Leu | Val | Gln | Lys | Val | Gly |
|     |     |       |     | 245 |       |     |     |     | 250     |     |     |     |     | 255 |     |
| Phe | Phe | Gly   | Ile | Leu | Ala   | Cys | Ala | Ser | Ile     | Pro | Asn | Pro | Leu | Phe | Asp |
|     |     |       | 260 | )   |       |     |     | 265 | i       |     |     |     | 270 |     |     |
| Leu | Ala | Gly   | Ile | Thr | Cys   | Gly | His | Phe | Leu     | Val | Pro | Phe | Trp | Thr | Phe |
|     |     | 275   | ;   |     |       |     | 280 |     |         |     |     | 285 | ı   |     |     |
| Phe | Glv | , Als | Thr | Leu | ı Ile | Glv | Lvs | Ala | ر<br>He | He  | Lvs | Met | His | He  | Gln |

Lys Ile Phe Val Ile Ile Thr Phe Ser Lys His Ile Val Glu Gln Met Val Ala Phe Ile Gly Ala Val Pro Gly Ile Gly Pro Ser Leu Gln Lys Pro Phe Gln Glu Tyr Leu Glu Ala Gln Arg Gln Lys Leu His His Lys Ser Glu Met Gly Thr Pro Gln Gly Glu Asn Trp Leu Ser Trp Met Phe Glu Lys Leu Val Val Wet Val Cys Tyr Phe Ile Leu Ser Ile Ile Asn Ser Met Ala Gln Ser Tyr Ala Lys Arg Ile Gln Gln Arg Leu Asn Ser Glu Glu Lys Thr Lys <210> 125 <211> 453 <212> PRT <213> Homo sapiens <400> 125 Met Gly Val Leu Gly Arg Val Leu Leu Trp Leu Gln Leu Cys Ala Leu Thr Gln Ala Val Ser Lys Leu Trp Val Pro Asn Thr Asp Phe Asp Val

| Ala | Ala   | Asn | Trp  | Ser | Gln | Asn | Arg | Thr | Pro        | Cys | Ala | Gly | Gly | Ala | Val  |
|-----|-------|-----|------|-----|-----|-----|-----|-----|------------|-----|-----|-----|-----|-----|------|
|     |       | 35  |      |     |     |     | 40  |     |            |     |     | 45  |     |     |      |
| Glu | Phe   | Pro | Ala  | Asp | Lys | Met | Val | Ser | Val        | Leu | Val | Gln | Glu | Gly | His  |
|     | 50    |     |      |     |     | 55  |     |     |            |     | 60  |     |     |     |      |
| Ala | Val   | Ser | Asp  | Met | Leu | Leu | Pro | Leu | Asp        | Gly | Glu | Leu | Val | Leu | Ala  |
| 65  |       |     |      |     | 70  |     |     |     |            | 75  |     |     |     |     | 80   |
| Ser | Gly   | Ala | G1 y | Phe | Gly | Val | Ser | Asp | Val        | Gly | Ser | His | Leu | Asp | Cys  |
|     |       |     |      | 85  |     |     |     |     | 90         |     |     |     |     | 95  |      |
| Gly | Ala   | Gly | Glu  | Pro | Ala | Val | Phe | Arg | Asp        | Ser | Asp | Arg | Phe | Ser | Trp  |
|     |       |     | 100  |     |     |     |     | 105 |            |     |     |     | 110 |     |      |
| His | Asp   | Pro | His  | Leu | Trp | Arg | Ser | Gly | Asp        | Glu | Ala | Pro | Gly | Leu | Phe  |
|     |       | 115 |      |     |     |     | 120 |     |            |     |     | 125 |     |     |      |
| Phe | Val   | Asp | Λla  | Glu | Arg | Val | Pro | Cys | Arg        | His | Asp | Asp | Val | Phe | Phe  |
|     | 130   |     |      |     |     | 135 |     |     |            |     | 140 |     |     |     |      |
| Pro | Pro   | Ser | Ala  | Ser | Phe | Arg | Val | Gly | Leu        | Gly | Pro | Gly | Ala | Ser | Pro  |
| 145 |       |     |      |     | 150 |     |     |     |            | 155 |     |     |     |     | 160  |
| Val | Arg   | Val | Arg  | Ser | Ile | Ser | Ala | Leu | G1 y       | Arg | Thr | Phe | Thr | Arg | Asp  |
|     |       |     |      | 165 |     |     |     |     | 170        |     |     |     |     | 175 |      |
| Glu | Asp   | Leu | Ala  | Val | Phe | Leu | Ala | Ser | Arg        | Ala | Gly | Arg | Leu | Arg | Phe  |
|     |       |     | 180  |     |     |     |     | 185 |            |     |     |     | 190 |     |      |
| His | Gly   | Pro | Gly  | Ala | Leu | Ser | Val | Gly | Pro        | Glu | Asp | Cys | Ala | Asp | Pro  |
|     |       | 195 |      |     |     |     | 200 |     |            |     |     | 205 |     |     |      |
| Ser | Gly   | Cys | Val  | Cys | Gly | Asn | Ala | Glu | Ala        | Gln | Pro | Trp | Ile | Cys | Ala  |
|     | 210   |     |      |     |     | 215 |     |     |            |     | 220 |     |     |     |      |
| Δla | ا منا | Lau | Glo  | Pro | Lou | C1v | Glv | Ara | نر<br>درکر | Dro | Gla | ۸۱۵ | ۸۱۵ | Cuc | u; c |

| <b>22</b> 5 |     |     |     |     | 230               |     |     |     |     | 235  |     |     |     |     | 240 |
|-------------|-----|-----|-----|-----|-------------------|-----|-----|-----|-----|------|-----|-----|-----|-----|-----|
| Ser         | Ala | Leu | Arg | Pro | Gl <sub>i</sub> n | Gly | Gln | Cys | Cys | Asp  | Leu | Cys | Gly | Ala | Val |
|             |     |     |     | 245 |                   |     |     |     | 250 |      |     |     |     | 255 |     |
| Val         | Leu | Leu | Thr | His | Gly               | Pro | Ala | Phe | Asp | Leu  | Glu | Arg | Tyr | Arg | Ala |
|             |     |     | 260 |     |                   |     |     | 265 |     |      |     |     | 270 |     |     |
| Arg         | Ile | Leu | Asp | Thr | Phe               | Leu | Gly | Leu | Pro | Gln  | Tyr | His | Gly | Leu | Gln |
|             |     | 275 |     |     |                   |     | 280 |     |     |      |     | 285 |     |     |     |
| Val         | Ala | Val | Ser | Lys | Val               | Pro | Arg | Ser | Ser | Arg  | Leu | Arg | Glu | Ala | Asp |
|             | 290 |     |     |     |                   | 295 |     |     |     |      | 300 |     |     |     |     |
| Thr         | Glu | Ile | Gln | Val | Val               | Leu | Val | Glu | Asn | Gly  | Pro | Glu | Thr | Gly | Gly |
| 305         |     |     |     |     | 310               |     |     |     |     | 315  |     |     |     |     | 320 |
| Ala         | Gly | Arg | Leu | Ala | Arg               | Ala | Leu | Leu | Ala | Asp  | Val | Ala | Glu | Asn | Gly |
|             |     |     |     | 325 |                   |     |     |     | 330 |      |     | •   | •   | 335 |     |
| Glu         | Ala | Leu | Gly | Val | Leu               | Glu | Ala | Thr | Met | Arg  | Glu | Ser | Gly | Ala | His |
|             |     |     | 340 |     |                   |     |     | 345 |     |      |     |     | 350 |     |     |
| Val         | Trp | Gly | Ser | Ser | Ala               | Ala | Gly | Leu | Ala | G1 y | Gly | Val | Ala | Ala | Ala |
|             |     | 355 |     |     |                   |     | 360 |     |     |      |     | 365 |     |     |     |
| Val         | Leu | Leu | Ala | Leu | Leu               | Val | Leu | Leu | Val | Ala  | Pro | Pro | Leu | Leu | Arg |
|             | 370 |     |     |     |                   | 375 |     |     |     |      | 380 |     |     |     |     |
| Arg         | Ala | Gly | Arg | Leu | Arg               | Trp | Arg | Arg | His | G1u  | Ala | Ala | Ala | Pro | Ala |
| 385         |     |     |     |     | 390               |     |     |     |     | 395  |     |     |     |     | 400 |
| Gly         | Ala | Pro | Leu | Gly | Phe               | Arg | Asn | Pro | Val | Phe  | Asp | Val | Thr | Ala | Ser |
|             |     |     |     | 405 |                   |     |     |     | 410 |      |     |     |     | 415 |     |
| Glu         | Glu | Leu | Pro | Leu | Pro               | Arg | Arg | Leu | Ser | Leu  | Val | Pro | Lys | Ala | Ala |
|             |     |     | 420 |     |                   |     |     | 425 |     |      |     |     | 430 |     |     |

Ala Asp Ser Thr Ser His Ser Tyr Phe Val Asn Pro Leu Phe Ala Gly

435

440

445

Ala Glu Ala Glu Ala

450

<210> 126

⟨211⟩ 59

<212> PRT

<213> Homo sapiens

**<400>** 126

Met Thr Ser Val Ser Thr Gln Leu Ser Leu Val Leu Met Ser Leu Leu

1

5

10

. 15

Leu Val Leu Pro Val Val Glu Ala Val Glu Ala Gly Asp Ala Ile Ala

20

25

30

Leu Leu Cly Val Val Leu Ser Ile Thr Gly Ile Cys Ala Cys Leu

35

40

45

Gly Val Tyr Ala Arg Lys Arg Asn Gly Gln Met

50

55

<210> 127

<211> 210

<212> PRT

<213> Homo sapiens

<400> 127

Met Ala Leu Pro Gln Met Cys Asp Gly Ser His Leu Ala Ser Thr Leu

| 1   |     |     |     | 5   |     |     |     |      | 10  |     |     |     |     | 15  |     |
|-----|-----|-----|-----|-----|-----|-----|-----|------|-----|-----|-----|-----|-----|-----|-----|
| Arg | Tyr | Cys | Met | Thr | Val | Ser | Gly | Thr  | Val | Val | Leu | Val | Ala | Gly | Thr |
|     |     |     | 20  |     |     |     |     | 25   |     |     |     |     | 30  |     |     |
| Leu | Cys | Phe | Ala | Trp | Trp | Ser | Glu | G1 y | Asp | Ala | Thr | Ala | Gln | Pro | Gly |
|     |     | 35  |     |     |     |     | 40  |      |     |     |     | 45  |     |     |     |
| Gln | Leu | Ala | Pro | Pro | Thr | Glu | Tyr | Pro  | Val | Pro | Glu | Gly | Pro | Ser | Pro |
|     | 50  |     |     |     |     | 55  |     |      |     |     | 60  |     |     |     |     |
| Leu | Leu | Arg | Ser | Val | Ser | Phe | Val | Cys  | Cys | Gly | Ala | Gly | Gly | Leu | Leu |
| 65  |     |     |     |     | 70  |     |     |      |     | 75  |     |     |     |     | 80  |
| Leu | Leu | Ile | Gly | Leu | Leu | Trp | Ser | Val  | Lys | Ala | Ser | Ile | Pro | Gly | Pro |
|     |     |     |     | 85  |     |     |     |      | 90  |     |     |     |     | 95  |     |
| Pro | Arg | Trp | Åsp | Pro | Tyr | His | Leu | Ser  | Arg | Asp | Leu | Tyr | Tyr | Leu | Thr |
|     |     |     | 100 |     |     |     |     | 105  |     |     |     |     | 110 |     |     |
| Val | Glu | Ser | Ser | Glu | Lys | Ģlu | Ser | Cys  | Arg | Thr | Pro | Lys | Val | Val | Asp |
|     |     | 115 |     |     |     |     | 120 |      |     |     |     | 125 |     |     |     |
| He  | Pro | Thr | Tyr | Glu | Glu | Ala | Val | Ser  | Phe | Pro | Val | Ala | Glu | Gly | Pro |
|     | 130 |     |     |     |     | 135 |     |      |     |     | 140 |     |     |     |     |
| Pro | Thr | Pro | Pro | Ala | Tyr | Pro | Thr | Glu  | Glu | Ala | Leu | Glu | Pro | Ser | Gly |
| 145 |     |     |     |     | 150 |     |     |      |     | 155 |     |     |     |     | 160 |
| Ser | Arg | Asp | Ala | Leu | Leu | Ser | Thr | Gln  | Pro | Ala | Trp | Pro | Pro | Pro | Ser |
|     |     |     |     | 165 |     |     |     |      | 170 |     |     |     | •   | 175 |     |
| Tyr | Glu | Ser | Ile | Ser | Leu | Ala | Leu | Asp  | Ala | Val | Ser | Ala | Glu | Thr | Thr |
|     |     |     | 180 |     |     |     |     | 185  |     |     |     |     | 190 |     |     |
| Pro | Ser | Ala | Thr | Arg | Ser | Cys | Ser | Gly  | Leu | Val | Gln | Thr | Ala | Arg | Gly |
|     |     | 195 |     |     |     |     | 200 |      |     |     |     | 205 |     |     |     |

Gly Ser 210 <210> 128 <211> 165 <212> PRT <213> Homo sapiens <400> 128 Met Asp Ser Ser Arg Ala Arg Gln Gln Leu Arg Arg Phe Leu Leu 5 10 15 Leu Pro Asp Ala Glu Ala Gln Leu Asp Arg Glu Gly Asp Ala Gly Pro 20 25 30 Glu Thr Ser Thr Ala Val Glu Lys Lys Glu Lys Pro Leu Pro Arg Leu 35 40 45 Asn Ile His Ser Gly Phe Trp Ile Leu Ala Ser Ile Val Val Thr Tyr 50 55 60 Tyr Val Asp Phe Phe Lys Thr Leu Lys Glu Asn Phe His Thr Ser Ser 70 65 75 80 Trp Phe Leu Cys Gly Ser Ala Leu Leu Leu Val Ser Leu Ser Ile Ala 85 90 95 Phe Tyr Cys Ile Val Tyr Leu Glu Trp Tyr Cys Gly Ile Gly Glu Tyr 100 105 110

Ala Ala Gly Ile Cys Phe Asn Ile Alá Leu Trp His Val Trp Ser Phe

Asp Val Lys Tyr Pro Ala Leu Ile Pro Ile Thr Thr Ala Ser Phe Ile

125

120

115

Phe Thr Pro Leu Leu Phe Thr Gln Phe Met Gly Val Val Met Phe Ile Thr Leu Leu Gly <210> 129 <211> 162 <212> PRT <213> Homo sapiens <400> 129 Met Leu Gln Thr Ser Asn Tyr Ser Leu Val Leu Ser Leu Gln Phe Leu Leu Leu Ser Tyr Asp Leu Phe Val Asn Ser Phe Ser Glu Leu Leu Gln Lys Thr Pro Val Ile Gln Leu Val Leu Phe Ile Ile Gln Asp Ile Ala Val Leu Phe Asn Ile Ile Ile Phe Leu Met Phe Phe Asn Thr Phe Val Phe Gln Ala Gly Leu Val Asn Leu Leu Phe His Lys Phe Lys Gly Thr Ile Ile Leu Thr Ala Val Tyr Phe Ala Leu Ser Ile Ser Leu His 

Val Trp Val Met Asn Leu Arg Trp Lys Asn Ser Asn Ser Phe Ile Trp

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Thr Asp Gly Leu Gln Met Leu Phe Val Phe Gln Arg Leu Ala Ala Val Leu Tyr Cys Tyr Phe Tyr Lys Arg Thr Ala Val Arg Leu Gly Asp Pro His Phe Tyr Gln Asp Ser Leu Trp Leu Arg Lys Glu Phe Met Gln Val Arg Arg <210> 130 <211> 221 <212> PRT <213> Homo sapiens <400> 130 Met Ala Leu Ala Leu Ala Ala Leu Ala Ala Val Glu Pro Ala Cys Gly l Ser Arg Tyr Gln Gln Leu Gln Asn Glu Glu Glu Ser Gly Glu Pro Glu Gln Ala Ala Gly Asp Ala Pro Pro Pro Tyr Ser Ser Ile Ser Ala Glu Ser Ala Ala Tyr Phe Asp Tyr Lys Asp Glu Ser Gly Phe Pro Lys Pro Pro Ser Tyr Asn Val Ala Thr Thr Leu Pro Ser Tyr Asp Glu Ala Glu Arg Thr Lys Ala Glu Ala Thr Ile Pro Leu Val Pro Gly Arg Asp Glu 

| Asp | Phe | Val | Gly | Arg | Asp | Asp | Phe | Asp | Asp | Ala | Asp | Gln | Leu | Arg | Ile |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
|     |     |     | 100 |     |     |     |     | 105 |     |     |     |     | 110 | •   |     |
| Gly | Asn | Asp | Gly | Ile | Phe | Met | Leu | Thr | Phe | Phe | Met | Ala | Phe | Leu | Phe |
|     |     | 115 |     |     |     |     | 120 |     |     |     |     | 125 |     |     |     |
| Asn | Trp | Ile | Gly | Phe | Phe | Leu | Ser | Phe | Cys | Leu | Thr | Thr | Ser | Ala | Ala |
|     | 130 |     |     |     |     | 135 |     |     |     |     | 140 |     |     |     |     |
| G1y | Arg | Tyr | Gly | Ala | Ile | Ser | Gly | Phe | Gly | Leu | Ser | Leu | Ile | Lys | Trp |
| 145 |     |     |     |     | 150 |     |     |     |     | 155 |     |     |     |     | 160 |
| Ile | Leu | Ile | Val | Arg | Phe | Ser | Thr | Tyr | Phe | Pro | Gly | Tyr | Phe | Asp | Gly |
|     |     |     |     | 165 |     |     |     |     | 170 |     |     |     |     | 175 |     |
| G1n | Tyr | Trp | Leu | Trp | Trp | Val | Phe | Leu | Val | Leu | Gly | Phe | Leu | Leu | Phe |
|     |     |     | 180 |     |     |     |     | 185 |     |     |     |     | 190 |     |     |
| Leu | Arg | Gly | Phe | Ile | Asn | Tyr | Ala | Lys | Val | Arg | Lys | Met | Pro | Glu | Thr |
|     |     | 195 |     |     |     |     | 200 |     |     |     |     | 205 |     |     |     |
| Phe | Ser | Asn | Leu | Pro | Arg | Thr | Arg | Val | Leu | Phe | Ile | Tyr |     |     |     |
|     | 210 |     |     |     |     | 215 |     |     |     |     | 220 |     |     |     |     |
|     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |
|     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |

⟨210⟩ 131

<211> 1011

<212> DNA

<213> Homo sapiens

<400> 131

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| 240  | aaacaaaatc | tgtccaagct | atactatatg | caccataatg | agatggcagc | ggaattggac |
|------|------------|------------|------------|------------|------------|------------|
| 300  | gcctctcctc | tgtttcctct | cctgtaaagc | taagaaaatt | ctgattttga | attcacttcc |
| 360  | accgatgttc | aattaagcct | agcacaagta | tggattatca | accacataag | tacgttggaa |
| 420  | catacttggg | tggaaaccat | accttacttc | cattccactt | ggaaattcac | accgtgctca |
| 480  | ggctttcata | ttattctcgg | gtctttgcca | catcctcagt | cactcaacat | aagcagtatt |
| 540  | cctgaatgat | tttttgtatt | gaaggctata | ttttaactta | ctgaccttgc | gcagctgggt |
| 600  | ggagctaggg | tggacccaaa | aaacagaaaa | agtttatacc | cagcaaatgg | atcttcacag |
| 660  | tattattagt | tcccaactct | ttcatgatta | caatgcctgc | tacttttcta | aaatacggag |
| 720  | tgttgtgttt | aatggaagaa | gaattcaacc | acaggctact | gagacctgca | gtctccactg |
| 780  | cacggttctg | tgatgtactc | gggtttctgc | ctgttttttg | ttcttctttc | atcctacagt |
| 840  | gaatgtatcc | gagccatcaa | gcagtggttg | cctgacgaca | acaattcagc | tgcagctatt |
| 900  | aaactttgta | tctctttgtt | gactacattt | aatcggtgga | ttgggatatt | gttgcctaca |
| 960  | gagcagccag | ttttaacact | agatattcct | agggggcttg | tttgcatggc | gggttaaata |
| 1011 | С          | atttgaagag | atctgtttgg | tgaagaaaac | aacctgtggg | ttaaaaccta |

<210> 132

<211> 708

<212> DNA

<213> Homo sapiens

<400> 132

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| ctcgcattaa | tgctgcaaag | agactctgca | gatagtgaaa | aagatggagg | gccccaattt | 360 |
|------------|------------|------------|------------|------------|------------|-----|
| gcagaggtgt | ttgtcattgt | ctggtttggt | gcagttacca | tcaccctcaa | ctcaaaactt | 420 |
| cttggaggga | acatatcttt | ttttcagagc | ctctgtgtgc | tgggttactg | tatacttccc | 480 |
| ttgacagtag | caatgctgat | ttgccggctg | gtacttttgg | ctgatccagg | acctgtaaac | 540 |
| ttcatggttc | ggctttttgt | ggtgattgtg | atgtttgcct | ggtctatagt | tgcctccaca | 600 |
| gctttccttg | ctgatagcca | gcctccaaac | cgcagagccc | tagctgttta | tcctgttttc | 660 |
| ctgttttact | ttgtcatcag | ttggatgatt | ctcaccttta | ctcctcag   |            | 708 |

<210> 133

<211> 1680

<212> DNA

<213> Homo sapiens

<400> 133

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| cccaatcctg | tggcatacta | cctgcaccac | tcaccctggt | ggttccatcg | cttcgagacg | 780  |
|------------|------------|------------|------------|------------|------------|------|
| ctcagcaacc | acttcatcga | gctcctggtg | cccttcttcc | tcttcctcgg | ccggcgggcg | 840  |
| tgcatcatcc | acggggtgct | gcagatcctg | ttccaggccg | tcctcatcgt | cagcgggaac | 900  |
| ctcagcttcc | tgaactggct | gactatggtg | cccagcctgg | cctgctttga | tgacgccacc | 960  |
| ctgggattct | tgttcccctc | tgggccaggc | agcctgaagg | accgagttct | gcagatgcag | 1020 |
| agggacatcc | gaggggcccg | gcccgagccc | agattcggct | ccgtggtgcg | gcgtgcagcc | 1080 |
| aacgtctcgc | tgggcgtcct | gctggcctgg | ctcagcgtgc | ccgtggtcct | caacttgctg | 1140 |
| agctccaggc | aggtcatgaa | cacccacttc | aactctcttc | acatcgtcaa | cacttacggg | 1200 |
| gccttcggaa | gcatcaccaa | ggagcgggcg | gaggtgatcc | tgcagggcac | agccagetee | 1260 |
| aacgccagcg | ccccgatgc  | catgtgggag | gactacgagt | tcaagtgcaa | gccaggtgac | 1320 |
| cccagcagac | ggccctgcct | catctccccg | taccactacc | gcctggactg | gctgatgtgg | 1380 |
| ttcgcggcct | tccagaccta | cgagcacaac | gactggatca | tccacctggc | tggcaagctc | 1440 |
| ctggccagcg | acgccgaggc | cttgtccctg | ctggcacaca | accccttcgc | gggcaggccc | 1500 |
| ccgcccaggt | gggtccgagg | agagcactac | aggtacaagt | tcagccgtcc | tgggggcagg | 1560 |
| cacgccgccg | agggcaagtg | gtgggtgcgg | aagaggatcg | gagcctactt | ccctccgctc | 1620 |
| agcctggagg | agctgaggcc | ctacttcagg | gaccgtgggt | ggcctctgcc | cgggcccctc | 1680 |

<210> 134

<211> 1218

<212> DNA

<213> Homo sapiens

<400> 134

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| atccttgtaa | tcttgaagga | atggacctca | aaattatggc | atcgtcaaag | cattgtggtg | 240  |
|------------|------------|------------|------------|------------|------------|------|
| tcttttttac | tgctgcttgc | tgtgcttata | gctacgtatt | atgttgaagg | agtgcatcaa | 300  |
| cagtatgtgc | aacgtataga | gaaacagttt | cttttgtatg | cctactggat | aggcttagga | 360  |
| attttgtctt | ctgttgggct | tggaacaggg | ctgcacacct | ttctgcttta | tctgggtcca | 420  |
| catatagcct | cagttacatt | agctgcttat | gaatgcaatt | cagttaattt | tcccgaacca | 480  |
| ccctatcctg | atcagattat | ttgtccagat | gaagagggca | ctgaaggaac | catttctttg | 540  |
| tggagtatca | tctcaaaagt | taggattgaa | gcctgcatgt | ggggtatcgg | tacagcaatc | 600  |
| ggagagctgc | ctccatattt | catggccaga | gcagctcgcc | tctcaggtgc | tgaaccagat | 660  |
| gatgaagagt | atcaggaatt | tgaagagatg | ctggaacatg | cagagtctgc | acaagacttt | 720  |
| gcctcccggg | ccaaactggc | agttcaaaaa | ctagtacaga | aagttggatt | ttttggaatt | 780  |
| ttggcctgtg | cttcaattcc | aaatccttta | tttgatctgg | ctggaataac | gtgtggacac | 840  |
| tttctggtac | ctttttggac | cttctttggt | gcaaccctaa | ttggaaaagc | aataataaaa | 900  |
| atgcatatcc | agaaaatttt | tgttataata | acattcagca | agcacatagt | ggagcaaatg | 960  |
| gtggctttca | ttggtgctgt | ccccggcata | ggtccatctc | tgcagaagcc | atttcaggag | 1020 |
| tacctggagg | ctcaacggca | gaagcttcac | cacaaaagcg | aaatgggcac | accacaggga | 1080 |
| gaaaactggt | tgtcctggat | gtttgaaaag | ttggtcgttg | tcatggtgtg | ttacttcatc | 1140 |
| ctatctatca | ttaactccat | ggcacaaagt | tatgccaaac | gaatccagca | gcggttgaac | 1200 |
| tragaggaga | aaactaaa   |            |            |            |            | 1218 |

⟨210⟩ 135

<211> 1359

<212> DNA

<213> Homo sapiens

<400≻ 135

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| tccaaactct | gggtccccaa | cacggacttc | gacgtcgcag | ccaactggag | ccagaaccgg | 120  |
|------------|------------|------------|------------|------------|------------|------|
| accccgtgcg | ccggcggcgc | cgttgagttc | ccggcggaca | agatggtgtc | agtcctggtg | 180  |
| caagaaggtc | acgccgtctc | agacatgctc | ctgccgctgg | atggggaact | cgtcctggct | 240  |
| tcaggagccg | gattcggcgt | ctcagacgtg | ggctcgcacc | tggactgtgg | cgcgggcgaa | 300  |
| cctgccgtct | tccgcgactc | tgaccgcttc | tcctggcatg | acccgcacct | gtggcgctct | 360  |
| ggggacgagg | cacctggcct | cttcttcgtg | gacgccgagc | gcgtgccctg | ccgccacgac | 420  |
| gacgtcttct | ttccgcctag | tgcctccttc | cgcgtggggc | teggeeetgg | cgctagcccc | 480  |
| gtgcgtgtcc | gcagcatctc | ggctctgggc | cggacgttca | cgcgcgacga | ggacctggct | 540  |
| gttttcctgg | cgtcccgcgc | gggccgccta | cgcttccacg | ggccgggcgc | gctgagcgtg | 600  |
| ggccccgagg | actgcgcgga | cccgtcgggc | tgcgtctgcg | gcaacgcgga | ggcgcagccg | 660  |
| tggatctgcg | cggccctgct | ccagcccctg | ggcggccgct | gccccaggc  | cgcctgccac | 720  |
| agegeeetee | ggccccaggg | gcagtgctgt | gacctctgtg | gagccgttgt | gttgctgacc | 780  |
| cacggccccg | catttgacct | ggagcggtac | cgggcgcgga | tactggacac | cttcctgggt | 840  |
| ctgcctcagt | accacgggct | gcaggtggcc | gtgtccaagg | tgccacgctc | gtcccggctc | 900  |
| cgtgaggccg | atacggagat | ccaggtggtg | ctggtggaga | atgggcccga | gacaggcgga | 960  |
| gcggggcggc | tggcccgggc | cctcctggcg | gacgtcgccg | agaacggcga | ggccctcggc | 1020 |
| gtcctggagg | cgaccatgcg | ggagtcgggc | gcacacgtct | ggggcagctc | cgcggctggg | 1080 |
| ctggcgggcg | gcgtggcggc | tgccgtgctg | ctggcgctgc | tggtcctgct | ggtggcgccg | 1140 |
| ccgctgctgc | gccgcgcggg | gaggctcagg | tggaggaggc | acgaggcggc | ggccccggct | 1200 |
| ggagcgcccc | tcggcttccg | caacccggtg | ttcgacgtga | cggcctccga | ggagctgccc | 1260 |
| ctgccgcggc | ggctcagcct | ggttccgaag | gcggccgcag | acagcaccag | ccacagttac | 1320 |
| ttcgtcaacc | ctctgttcgc | cggggccgag | gccgaggcc  |            |            | 1359 |

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<212> DNA

<213> Homo sapiens

<400> 136

| at | gacctcag | tttcaacaca | gttgtcctta | gtcctcatgt | cactgctttt | ggtgctgcct | 60  |
|----|----------|------------|------------|------------|------------|------------|-----|
| gt | tgtggaag | cagtagaagc | cggtgatgca | atcgcccttt | tgttaggtgt | ggttctcagc | 120 |
| at | tacaggca | tttgtgcctg | cttgggggta | tatgcacgaa | aaagaaatgg | acagatg    | 177 |
| at | gacctcag | tttcaacaca | gttgtcctta | gtcctcatgt | cactgctttt | ggtgctgcct | 60  |
| gt | tgtggaag | cagtagaagc | cggtgatgca | atcgcccttt | tgttaggtgt | ggttctcagc | 120 |
| at | tacaggca | tttgtgcctg | cttgggggta | tatgcacgaa | aaagaaatgg | acagatg    | 177 |

<210> 137

<211> 630

<212> DNA

<213> Homo sapiens

<400> 137

60 atggecetge eccagatgtg tgacgggage caettggeet ecaeceteeg etattgeatg 120 acagtcagcg gcacagtggt tctggtggcc gggacgctct gcttcgcttg gtggagcgaa 180 ggggatgcaa ccgcccagcc tggccagctg gccccaccca cggagtatcc ggtgcctgag 240 ggccccagcc ccctgctcag gtccgtcagc ttcgtctgct gcggtgcagg tggcctgctg 300 ctgctcattg gcctgctgtg gtccgtcaag gccagcatcc cagggccacc tcgatgggac 360 ccctatcacc tctccagaga cctgtactac ctcactgtgg agtcctcaga gaaggagagc 420 tgcaggaccc ccaaagtggt tgacatcccc acttacgagg aagccgtgag cttcccagtg 480 gccgaggggc ccccaacacc acctgcatac cctacggagg aagccctgga gccaagtgga 540 tcgagggatg ccctgctcag cacccagccc gcctggcctc cacccagcta tgagagcatc agcettgete tigatgeegt tietgeagag acgaeacega gigeeacaeg etectgetea 600

| ggcct | ggttc | agactgcacg | gggaggaagt |            |            |            | 630 |
|-------|-------|------------|------------|------------|------------|------------|-----|
|       |       |            |            |            |            |            |     |
| <210> | 138   |            | •          |            |            |            |     |
| <211> | 495   |            |            | •          |            |            |     |
| <212> | DNA   |            |            |            |            |            |     |
| <213> | Homo  | sapiens    |            |            |            |            |     |
| <400> | 138   |            |            |            |            |            |     |
| atgga | ctcct | cgcgggcccg | acagcagctc | cggcggcgat | tcctcctcct | gccggacgcc | 60  |
| gaggc | ccagc | tggaccgcga | gggtgacgcc | gggccggaaa | cctccacagc | tgttgagaaa | 120 |
| aagga | gaaac | ctcttccaag | acttaatatc | cattctggat | tctggatttt | ggcatccatt | 180 |
| gttgt | gacct | attatgttga | cttctttaaa | acccttaaag | aaaacttcca | cactagcagc | 240 |
| tggtt | tctct | gtggcagtgc | cttgttgctt | gtcagtttat | caattgcatt | ttactgcata | 300 |
| gtcta | cctgg | aatggtattg | tggaattgga | gaatatgatg | tcaagtatcc | agccttgata | 360 |
| cccat | tacca | ctgcctcctt | tattgcagca | ggaatttgct | tcaacattgc | tttatggcat | 420 |
| gtgtg | gtcgt | ttttcactcc | attgttgttg | tttacccagt | ttatgggggt | tgtcatgttt | 480 |
| atcac | actcc | ttgga      |            |            |            |            | 495 |
|       |       |            |            |            |            |            |     |
| <210> | 139   | ·          |            |            |            |            |     |
| <211> | 486   |            |            |            |            |            |     |
| <212> | DNA   |            |            |            |            |            |     |
| <213> | Homo  | sapiens    |            |            |            |            |     |
| <400> | 139   |            |            |            |            |            | i   |
| atgct | ccaga | ccagtaacta | cagcctggtg | ctctctctgc | agttcctgct | gctgtcctat | 60  |
| gacct | ctttg | tcaattcctt | ctcagaactg | ctccaaaaga | ctcctgtcat | ccagcttgtg | 120 |
| ctctt | catca | tccaggatat | tgcagtcctc | ttcaacatca | tcatcatttt | cctcatgttc | 180 |

| ttcaacacct | tcgtcttcca | ggctggcctg | gtcaacctcc | tattccataa | gttcaaaggg | 240 |
|------------|------------|------------|------------|------------|------------|-----|
| accatcatcc | tgacagctgt | gtactttgcc | ctcagcatct | cccttcatgt | ctgggtcatg | 300 |
| aacttacgct | ggaaaaactc | caacagcttc | atatggacag | atggacttca | aatgctgttt | 360 |
| gtattccaga | gactagcagc | agtgttgtac | tgctacttct | ataaacggac | agccgtaaga | 420 |
| ctaggcgatc | ctcacttcta | ccaggactct | ttgtggctgc | gcaaggagtt | catgcaagtt | 480 |
| cgaagg     |            |            |            |            |            | 486 |

<210> 140

<211> 663

<212> DNA

<213> Homo sapiens

<400> 140

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| <210  | > 141 |     |       |       |       |       |       |       |       |              |     |              |     |       |       |    |     |
|-------|-------|-----|-------|-------|-------|-------|-------|-------|-------|--------------|-----|--------------|-----|-------|-------|----|-----|
| <2112 | > 162 | 2   |       |       |       |       |       |       |       |              |     |              |     |       |       |    |     |
| <212  | > DNA |     |       |       |       |       |       |       |       |              |     |              |     |       |       |    |     |
| <213  | > Hom | o s | apie  | ens   |       |       |       |       |       |              |     |              |     |       |       |    |     |
| <220  | >     |     |       |       |       |       |       |       |       |              |     |              |     |       |       |    |     |
| <2212 | > CDS |     |       |       |       |       |       |       |       |              |     |              |     |       |       |    |     |
| <222  | > (78 | )   | . (10 | 91)   |       |       |       |       |       |              |     |              |     |       |       |    |     |
| <400  | > 141 |     |       |       |       |       |       |       |       |              |     |              |     |       |       |    |     |
| ctcti | tcccc | g g | ccce  | gccg  | gg go | cggg  | acca  | g tgo | egea  | gccg         | ggg | ctgg         | cgg | gcgg  | cgggg | ţt | 60  |
| ccgcg | ggggc | c g | cage  | gag a | atg a | acg ( | gcc   | ggc ( | ggc ( | cag g        | gcc | gag (        | gcc | gag   | ggc   |    | 110 |
|       |       |     |       | λ     | let ´ | Thr i | Ala ( | Gly ( | Gly ( | Gln <i>I</i> | Ala | Glu <i>i</i> | Ala | Glu ( | Gly   |    |     |
|       |       |     |       |       | 1     |       |       |       | 5     |              |     |              |     | 10    |       |    |     |
| gct g | ggc g | gg  | gag   | ccc   | ggc   | gcg   | gcg   | cgg   | ctg   | ссс          | tcg | cgg          | gtg | gcc   | cgg   |    | 158 |
| Ala ( | Gly G | l y | Glu   | Pro   | Gly   | Ala   | Ala   | Arg   | Leu   | Pro          | Ser | Arg          | Val | Ala   | Arg   |    |     |
|       |       |     | 15    |       |       |       |       | 20    |       |              |     |              | 25  |       | •     |    |     |
| ctg   | ctg t | cg  | gcg   | ctc   | ttc   | tac   | ggg   | acc   | tgc   | tcc          | ttc | ctc          | atc | gtg   | ctt   | :  | 206 |
| Leu l | Leu S | er  | Ala   | Leu   | Phe   | Tyr   | Gly   | Thr   | Cys   | Ser          | Phe | Leu          | Ile | Val   | Leu   |    |     |
|       |       | 30  |       |       |       |       | 35    |       |       |              |     | 40           |     |       |       |    |     |
| gtc a | aac a | ag  | gcg   | ctg   | ctg   | acc   | acc   | tac   | ggt   | ttc          | ccg | tca          | cca | att   | ttc   | 2  | 254 |
| Val / | Asn L | ys. | Ala   | Leu   | Leu   | Thr   | Thr   | Tyr   | Gly   | Phe          | Pro | Ser          | Pro | Ile   | Phe   |    |     |
|       | 45    |     |       |       |       | 50    |       |       |       |              | 55  |              |     |       |       |    |     |
| ctt į | gga a | tt  | gga   | cag   | atg   | gca   | gcc   | acc   | ata   | atg          | ata | cta          | tat | gtg   | tcc   | ;  | 302 |
| Leu ( | Gly I | le  | Gly   | Gln   | Met   | Ala   | Ala   | Thr   | Ile   | Met          | Ile | Leu          | Tyr | Val   | Ser   |    |     |
| 60    |       |     |       |       | 65    |       |       |       |       | 70           |     |              |     |       | 75    |    |     |
| aag o | cta a | ac  | aaa   | atc   | att   | cac   | ttc   | cct   | gat   | ttt          | gat | aag          | aaa | att   | cct   | ;  | 350 |

| Lys | Leu | Asn | Lys | Ile | Ile | His | Phe | Pro | Asp | Phe | Asp | Lys | Lys | Ile | Pro |     |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
|     |     |     |     | 80  |     |     |     |     | 85  |     |     |     |     | 90  |     |     |
| gta | aag | ctg | ttt | cct | ctg | cct | ctc | ctc | tac | gtt | gga | aac | cac | ata | agt | 398 |
| Val | Lys | Leu | Phe | Pro | Leu | Pro | Leu | Leu | Tyr | Val | Gly | Asn | His | Ile | Ser |     |
|     |     |     | 95  |     |     |     |     | 100 |     |     |     |     | 105 |     |     |     |
| gga | tta | tca | agc | aca | agt | aaa | tta | agc | cta | ccg | atg | ttc | acc | gtg | ctc | 446 |
| Gly | Leu | Ser | Ser | Thr | Ser | Lys | Leu | Ser | Leu | Pro | Met | Phe | Thr | Val | Leu |     |
|     |     | 110 |     |     |     |     | 115 |     |     |     |     | 120 |     |     |     |     |
| agg | aaa | ttc | acc | att | cca | ctt | acc | tta | ctt | ctg | gaa | acc | atc | ata | ctt | 494 |
| Arg | Lys | Phe | Thr | Ile | Pro | Leu | Thr | Leu | Leu | Leu | Glu | Thr | Ile | Ile | Leu |     |
|     | 125 |     |     |     |     | 130 |     |     |     |     | 135 |     |     |     |     |     |
| ggg | aag | cag | tat | tca | ctc | aac | atc | atc | ctc | agt | gtc | ttt | gcc | att | att | 542 |
| Gly | Lys | Gln | Tyr | Ser | Leu | Asn | Ile | Ile | Leu | Ser | Val | Phe | Ala | Ile | Ile |     |
| 140 |     |     |     |     | 145 |     |     |     |     | 150 |     |     |     |     | 155 |     |
| ctc | ggg | gct | ttc | ata | gca | gct | ggg | tct | gac | ctt | gct | ttt | aac | tta | gaa | 590 |
| Leu | Gly | Ala | Phe | Ile | Ala | Ala | Gly | Ser | Asp | Leu | Ala | Phe | Asn | Leu | Glu |     |
|     |     |     |     | 160 |     |     |     |     | 165 |     |     |     |     | 170 |     |     |
| ggc | tat | att | ttt | gta | ttc | ctg | aat | gat | atc | ttc | aca | gca | gca | aat | gga | 638 |
| Gly | Tyr | Ile | Phe | Val | Phe | Leu | Asn | Asp | Ile | Phe | Thr | Ala | Ala | Asn | Gly |     |
|     |     |     | 175 |     |     |     |     | 180 |     |     |     |     | 185 |     |     |     |
| gtt | tat | acc | aaa | cag | aaa | atg | gac | cca | aag | gag | cta | ggg | aaa | tac | gga | 686 |
| Val | Tyr | Thr | Lys | Gln | Lys | Met | Asp | Pro | Lys | Glu | Leu | Gly | Lys | Tyr | Gly |     |
|     |     | 190 |     |     |     |     | 195 |     |     |     |     | 200 |     |     |     |     |
| gta | ctt | ttc | tac | aat | gcc | tgc | ttc | atg | att | atc | cca | act | ctt | att | att | 734 |
| Val | Leu | Phe | Tyr | Asn | Ala | Cys | Phe | Met | Ile | Ile | Pro | Thr | Leu | Ile | Ile |     |

|     | 205 |     |     |     |     | 210  |      |       |       |       | 215   |       |       |      |     |      |
|-----|-----|-----|-----|-----|-----|------|------|-------|-------|-------|-------|-------|-------|------|-----|------|
| agt | gtc | tcc | act | gga | gac | ctg  | caa  | cag   | gct   | act   | gaa   | tţc   | aac   | caa  | tgg | 782  |
| Ser | Val | Ser | Thr | Gly | Asp | Leu  | Gln  | Gln   | Ala   | Thr   | Glu   | Phe   | Asn   | Gln  | Trp |      |
| 220 |     |     |     |     | 225 |      |      |       |       | 230   |       |       |       |      | 235 |      |
| aag | aat | gtt | gtg | ttt | atc | cta  | cag  | ttt   | ctt   | ctt   | tcc   | tgt   | ttt   | ttg  | ggg | 830  |
| Lys | Asn | Val | Val | Phe | Ile | Leu  | Gln  | Phe   | Leu   | Leu   | Ser   | Cys   | Phe   | Leu  | Gly |      |
|     |     |     |     | 240 |     |      |      |       | 245   |       |       |       |       | 250  |     |      |
| ttt | ctg | ctg | atg | tac | tcc | acg  | gtt  | ctg   | tgc   | agc   | tat   | tac   | aat   | tca  | gcc | 878  |
| Phe | Leu | Leu | Met | Tyr | Ser | Thr  | Val  | Leu   | Cys   | Ser   | Tyr   | Tyr   | Asn   | Ser  | Ala |      |
|     |     |     | 255 |     |     |      |      | 260   |       |       |       |       | 265   |      |     |      |
| ctg | acg | aca | gca | gtg | gtt | gga  | gcc  | atc   | aag   | aat   | gta   | tcc   | gtt   | gcc  | tac | 926  |
| Leu | Thr | Thr | Ala | Val | Val | Gly  | Ala  | Ile   | Lys   | Asn   | Val   | Ser   | Val   | Ala  | Tyr |      |
|     |     | 270 |     |     |     |      | 275  |       |       |       |       | 280   |       |      |     |      |
| att | ggg | ata | tta | atc | ggt | gga  | gac  | tac   | att   | ttc   | tct   | ttg   | tta   | aac  | ttt | 974  |
| Ile | Gly | He  | Leu | Ile | Gly | Gly  | Asp  | Tyr   | Ile   | Phe   | Ser   | Leu   | Leu   | Asn  | Phe |      |
|     | 285 |     |     |     |     | 290  |      |       |       |       | 295   |       |       |      |     |      |
| gta | ggg | tta | aat | att | tgc | atg  | gca  | ggg   | ggc   | ttg   | aga   | tat   | tcc   | ttt  | tta | 1022 |
| Val | Gly | Leu | Asn | Ile | Cys | Met  | Ala  | Gly   | Gly   | Leu   | Arg   | Tyr   | Ser   | Phe  | Leu |      |
| 300 |     |     |     |     | 305 |      |      |       |       | 310   |       |       |       |      | 315 |      |
| aca | ctg | agc | agc | cag | tta | aaa  | cct  | aaa   | cct   | gtg   | ggt   | gaa   | gaa   | aac  | atc | 1070 |
| Thr | Leu | Ser | Ser | Gln | Leu | Lys  | Pro  | Lys   | Pro   | Val   | Gly   | Glu   | Glu   | Asn  | Ile |      |
|     |     |     |     | 320 |     |      |      |       | 325   |       |       |       |       | 330  |     |      |
| tgt | ttg | gat | ttg | aag | agc | ta a | agag | gtctg | gc ag | gcagg | gatte | g gag | gacte | gact |     | 1120 |
| Cys | Leu | Asp | Leu | Lys | Ser |      |      |       |       |       |       |       |       |      |     |      |

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| tgtgactgcg | ggctgggggg | gcattcccag | taggaatgtg | aagccagagg | tttcggattc | 1180 |
|------------|------------|------------|------------|------------|------------|------|
| gtgacatcca | cccctgggc  | aagtgagagc | atctgcaaaa | tgcaaagaga | actacctcat | 1240 |
| atgcaggatg | agccaatggc | agtctcaaga | aatgtactcg | ggcgacacct | tacctgtgga | 1300 |
| aagcaaatct | tttcaaaata | agccactggg | actcggtagg | tggagcccca | gctgctcttc | 1360 |
| tagggaccta | tggggccttc | gtggcatctc | tgtgctgtgt | gctggggagg | aggttgatgt | 1420 |
| aatggtgact | cttttctgat | cagcaccttg | gccgtgattc | ccaaggtccc | agccaaagca | 1480 |
| aagggccagt | tgtttcagtt | taaacagaca | tgtctttagt | ctaataaaat | tagttaactg | 1540 |
| ccagtaaagt | tatttgttag | ctttgatgaa | agctatgttg | gtatctttcc | ctaatcatca | 1600 |
| aagtaaataa | aaaatcattt | ct         |            |            |            | 1622 |

<210> 142

<211> 2475

<212> DNA

<213> Homo sapiens

<220>

<221> CDS

⟨222⟩ (36)... (746)

<400> 142

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Met Ala Glu Ala Glu Glu

1

tct cca gga gac ccg ggg aca gca tcg ccc agg ccc ctg ttt gca ggc 101
Ser Pro Gly Asp Pro Gly Thr Ala Ser Pro Arg Pro Leu Phe Ala Gly

10 15 20

ctt tca gat ata tcc atc tca caa gac atc ccc gta gaa gga gaa atc 149

| Leu  | Ser | Asp | Ile | Ser | Ile | Ser | Gln | Asp | Ile | Pro | Val | Glu | Gly | Glu | Ile  |     |
|------|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|------|-----|
|      |     | 25  |     |     | •   |     | 30  |     |     |     |     | 35  |     |     |      |     |
| acc  | att | cct | atg | aga | tct | cgc | atc | cgg | gag | ttt | gac | agc | tcc | aca | tta  | 197 |
| Thr  | Ile | Pro | Met | Arg | Ser | Arg | Ile | Arg | Glu | Phe | Asp | Ser | Ser | Thr | Leu  |     |
|      | 40  |     |     |     |     | 45  |     |     |     |     | 50  |     |     |     |      |     |
| aat  | gaa | tct | gtt | cgc | aat | acc | atc | atg | cgt | gat | cta | aaa | gct | gtt | ggg  | 245 |
| Asn  | Glu | Ser | Val | Arg | Asn | Thr | Ile | Met | Arg | Asp | Leu | Lys | Ala | Val | Gly  |     |
| 55   |     |     |     |     | 60  |     |     |     |     | 65  |     |     |     |     | 70   |     |
| aaa  | aaa | ttc | atg | cat | gtt | ttg | tac | cca | agg | aaa | agt | aat | act | ctt | ttg  | 293 |
| Lys  | Lys | Phe | Met | His | Val | Leu | Tyr | Pro | Arg | Lys | Ser | Asn | Thr | Leu | Leu  |     |
|      |     |     |     | 75  |     |     |     |     | 80  |     |     |     | r   | 85  |      |     |
| aga  | gat | tgg | gat | ttg | tgg | ggc | cct | ttg | atc | ctt | tgt | gtg | aca | ctc | gca  | 341 |
| Arg  | Asp | Trp | Asp | Leu | Trp | Gly | Pro | Leu | Ile | Leu | Cys | Val | Thr | Leu | Ala  |     |
|      |     |     | 90  |     |     |     |     | 95  |     |     |     |     | 100 |     |      |     |
| tta  | atg | ctg | caa | aga | gac | tct | gca | gat | agt | gaa | aaa | gat | gga | ggg | ccc  | 389 |
| Leu  | Met | Leu | Gln | Arg | Asp | Ser | Ala | Asp | Ser | Glu | Lys | Asp | Gly | Gly | Pro  |     |
|      |     | 105 |     |     |     |     | 110 |     |     |     |     | 115 |     |     |      |     |
| caa  | ttt | gca | gag | gtg | ttt | gtc | att | gtc | tgg | ttt | ggt | gca | gtt | acc | atc  | 437 |
| Gln  | Phe | Ala | Glu | Val | Phe | Val | Ile | Val | Trp | Phe | Gly | Ala | Val | Thr | Ile  |     |
|      | 120 |     |     |     |     | 125 |     |     |     |     | 130 |     |     |     |      |     |
| acc  | ctc | aac | tca | aaa | ctt | ctt | gga | ggg | aac | ata | tct | ttt | ttt | cag | agc  | 485 |
| Thr  | Leu | Asn | Ser | Lys | Leu | Leu | Gly | Gly | Asn | Ile | Ser | Phe | Phe | Gln | Ser  |     |
| 135  |     |     |     |     | 140 |     |     |     |     | 145 |     |     |     |     | 150  |     |
| ctc  | tgt | gtg | ctg | ggt | tac | tgt | ata | ctt | ccc | ttg | aca | gta | gca | atg | ctg  | 533 |
| l eu | Cvs | Val | Leu | Glv | Tvr | Cvs | Πe  | Leu | Pro | Leu | Thr | Val | Ala | Met | l.eu |     |

| 155                 | i             | 160              | 165                |      |
|---------------------|---------------|------------------|--------------------|------|
| att tgc cgg ctg gta | ctt ttg gct   | gat cca gga cct  | gta aac ttc atg    | 581  |
| Ile Cys Arg Leu Val | Leu Leu Ala   | Asp Pro Gly Pro  | Val Asn Phe Met    |      |
| 170                 |               | 175              | 180                |      |
| gtt cgg ctt ttt gtg | gtg att gtg   | atg ttt gcc tgg  | tct ata gtt gcc    | 629  |
| Val Arg Leu Phe Val | Val Ile Val   | Met Phe Ala Trp  | Ser Ile Val Ala    |      |
| 185                 | 190           | •                | 195                |      |
| tcc aca gct ttc ctt | gct gat agc   | cag cct cca aac  | cgc aga gcc cta    | 677  |
| Ser Thr Ala Phe Leu | Ala Asp Ser   | Gln Pro Pro Asn  | Arg Arg Ala Leu    |      |
| 200                 | 205           | 210              |                    |      |
| gct gtt tat cct gtt | ttc ctg ttt   | tac ttt gtc atc  | agt tgg atg att    | 725  |
| Ala Val Tyr Pro Val | Phe Leu Phe   | Tyr Phe Val Ile  | Ser Trp Met Ile    |      |
| 215                 | 220           | 225              | 230                |      |
| ctc acc ttt act cct | cag taaatca   | ggaatgggaa atta  | aaaacc agtgaattga  | 780  |
| Leu Thr Phe Thr Pro | Gln           |                  |                    |      |
| 235                 |               |                  |                    |      |
| aagcacatct gaaagatg | ca attcaccate | g gagetttgte tet | ggccctt atttgtctaa | 840  |
| ttttggaggt atttgata | ac tgagtaggtg | g aggagattaa aag | ggagcca tatagcactg | 900  |
| tcacccctta tttgagga | ac tgatgtttga | aaggctgttc ttt   | tetetet taatgteatt | 960  |
| tctttaaaaa tacatgtg | ca tactacacac | agtatataat gcc   | tccttaa ggcatgatgg | 1020 |
| agtcaccgtg gtccattt | gg gtgacaacca | ı gtgacttggg aag | cacatag atacatetta | 1080 |
| caagttgaat agagttga | ta actatttca  | ı gttttgagaa tac | cagttca ggtgcagctc | 1140 |
| ttaaacacat tgccttat | ga ctattagaat | atgeetetet ttt   | cataaat aaaaatacat | 1200 |
| ggtctatatc cattttct | tt tatttetete | tettaagett aaa   | aaggcaa tgagagaggt | 1260 |
| taggagtggg ttcataca | cg gagaatgaga | ı aaacatgcat taa | ccaatat tcagatittg | 1320 |

| atcaggggaa | attctacact | tgttgcaaaa | aaaaaaaaa  | aaaaagcaaa | gggcctctaa | 1380 |
|------------|------------|------------|------------|------------|------------|------|
| agaatcagcc | tctttggtcc | ctttgtgctg | tcaccttttt | gccatgttta | acagcatctt | 1440 |
| ggttggcact | ctagtcttaa | tcttgctcct | taactttgaa | tatgcagtct | aaaatgtcag | 1500 |
| tagtcaacat | gtaattttcc | tttgaaattc | tgaatattcc | agtgctggaa | cttatccaaa | 1560 |
| aagaagacct | cagaaactta | gattggtaga | tctctagtgc | atattatcat | gtgggcacct | 1620 |
| tctcttaggg | tggaatgagg | cagtctggat | gcagcatagt | taaaaggagc | tgtttaatat | 1680 |
| tctctgtagt | ctggcctctt | aactagaaag | taaagctaaa | tcagaagcct | gtatttaacc | 1740 |
| atgtgaacag | ggagggattt | agtgttctga | tggctgatta | atagaacagc | tagatactta | 1800 |
| gagcatgacg | tgggatggga | tgagtttaca | gctgctgcct | tttcatggtg | agcttagcag | 1860 |
| ttttctcatt | agatgtgttt | ttttgggttg | gggaatagca | atttatttta | ttgattttag | 1920 |
| actttatcaa | gctaattagc | tcccctttag | ataagtacat | gttgcacatg | tgcacctact | 1980 |
| tgtaatctca | gatatttatg | cacacaagtg | tgaaggtttt | tcagggagca | gagcatctgg | 2040 |
| gacaggctga | ttctgagcta | aacagggctc | ctttaaggca | atatgaactg | ttgccttcta | 2100 |
| taaattgcac | attgaggaac | tctaatagac | aaagattagg | tgtcaggcag | aaaacactca | 2160 |
| ttgtaaatat | actattagtt | gataaacata | ggactttett | attccccagt | ttttctttat | 2220 |
| catataattt | aaatatttat | tcattttgta | tttaaagact | acctacacat | agatatatga | 2280 |
| ttccaaagtc | atactttctc | catccccaca | ttagccaagt | gaatacaggg | ccaaatgggt | 2340 |
| tcttggaatg | ataataacaa | agcattacaa | agtgggtccc | cttggttcca | gccttgtcca | 2400 |
| gagtttttgg | ttatatattt | ctatttatta | caatttacct | tttaaattgt | aaaataaacc | 2460 |
| tttgtgtgga | cagag      |            |            |            |            | 2475 |

<210> 143

<211> 1739

<212> DNA

<213> Homo sapiens

Ç

| <22 | 0>   |      |      | •    |      |      |      |      |      |      |      |      |      |      |     |     |
|-----|------|------|------|------|------|------|------|------|------|------|------|------|------|------|-----|-----|
| <22 | 1> C | DS   |      |      |      |      |      |      |      |      |      |      |      |      |     |     |
| <22 | 2> ( | 21). | (1   | 703) |      |      |      |      |      |      |      |      |      |      | ٠   |     |
| <40 | 0> 1 | 43   |      |      |      |      |      |      |      |      |      |      |      |      |     |     |
| tgc | gccc | tga  | cago | ccaa | ca a | tg g | cg g | cg c | cc g | cg g | ag t | cg c | tg a | gg a | gg  | 50  |
|     |      |      |      |      | M    | et A | la A | la P | ro A | la G | lu S | er L | eu A | rg A | rg  |     |
|     |      |      |      |      |      | 1    |      |      |      | 5    |      |      |      |      | 10  |     |
| cgg | aag  | act  | ggg  | tac  | tcg  | gat  | ccg  | gag  | cct  | gag  | tcg  | ccg  | ccc  | gcg  | ccg | 98  |
| Arg | Lys  | Thr  | Gly  | Tyr  | Ser  | Asp  | Pro  | Glu  | Pro  | Glu  | Ser  | Pro  | Pro  | Ala  | Pro |     |
|     |      |      |      | 15   |      |      |      |      | 20   |      |      |      |      | 25   |     | 4   |
| ggg | cgt  | ggc  | ccc  | gca  | ggc  | tct  | ccg  | gcc  | cat  | ctc  | cac  | acg  | ggc  | acc  | ttc | 146 |
| Gly | Arg  | Gly  | Pro  | Ala  | Gly  | Ser  | Pro  | Ala  | His  | Leu  | His  | Thr  | Gly  | Thr  | Phe |     |
|     |      |      | 30   |      |      |      |      | 35   |      |      |      |      | 40   |      |     |     |
| tgg | ctg  | acc  | cgg  | atc  | gtg  | ctc  | ctg  | aag  | gcc  | cta  | gcc  | ttc  | gtg  | tac  | ttc | 194 |
| Trp | Leu  | Thr  | Arg  | He   | Val  | Leu  | Leu  | Lys  | Ala  | Leu  | Ala  | Phe  | Val  | Tyr  | Phe |     |
|     |      | 45   |      |      |      |      | 50   |      |      |      |      | 55   |      |      |     |     |
| gtg | gca  | ttc  | ctg  | gtg  | gct  | ttc  | cat  | cag  | aac  | aag  | cag  | ctc  | atc  | ggt  | gac | 242 |
| Val | Ala  | Phe  | Leu  | Val  | Ala  | Phe  | His  | Gln  | Asn  | Lys  | Gln  | Leu  | Ile  | Gly  | Λsp |     |
|     | 60   |      |      |      |      | 65   |      |      |      |      | 70   |      |      |      | -   |     |
| agg | ggg  | ctg  | ctt  | ccc  | tgc  | aga  | gtg  | ttc  | ctg  | aag  | aac  | ttc  | cag  | cag  | tac | 290 |
| Arg | Gly  | Leu  | Leu  | Pro  | Cys  | Arg  | Val  | Phe  | Leu  | Lys  | Asn  | Phe  | Gln  | Gln  | Tyr |     |
| 75  |      |      |      |      | 80   |      |      |      |      | 85   |      |      |      |      | 90  |     |
| ttc | cag  | gac  | agg  | acg  | agc  | tgg  | gaa  | gtc  | ttc  | agc  | tac  | atg  | ccc  | acc  | atc | 338 |
| Phe | Gln  | Asp  | Arg  | Thr  | Ser  | Trp  | Glu  | Val  | Phe  | Ser  | Tyr  | Met  | Pro  | Thr  | Ile |     |

| ctc | tgg | ctg | atg | gac | tgg | tca | gac | atg | aac | tcc | aac | ctg | gac  | ttg | ctg | 386 |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|------|-----|-----|-----|
| Leu | Trp | Leu | Met | Asp | Trp | Ser | Asp | Met | Asn | Ser | Asn | Leu | Asp  | Leu | Leu |     |
|     |     |     | 110 |     |     |     |     | 115 |     |     |     |     | 120  |     |     |     |
| gct | ctt | ctc | gga | ctg | ggc | atc | tcg | tct | ttc | gta | ctg | atc | acg  | ggc | tgc | 434 |
| Ala | Leu | Leu | Gly | Leu | Gly | Ile | Ser | Ser | Phe | Val | Leu | Ile | Thr  | Gly | Cys |     |
|     |     | 125 |     |     |     |     | 130 |     |     |     |     | 135 |      |     |     |     |
| gcc | aac | atg | ctt | çtc | atg | gct | gcc | ctg | tgg | ggc | ctc | tac | atg  | tcc | ctg | 482 |
| Ala | Asn | Met | Leu | Leu | Met | Ala | Ala | Leu | Trp | Gly | Leu | Tyr | Met  | Ser | Leu |     |
|     | 140 |     |     |     |     | 145 |     |     |     |     | 150 |     |      |     |     |     |
| gtt | aat | gtg | ggc | cat | gtc | tgg | tac | tct | ttc | gga | tgg | gag | tcc. | cag | ctt | 530 |
| Val | Asn | Val | Gly | His | Val | Trp | Tyr | Ser | Phe | Gly | Trp | Glu | Ser  | Gln | Leu |     |
| 155 |     |     |     |     | 160 |     |     |     |     | 165 |     |     |      |     | 170 |     |
| ctg | gag | acg | ggg | ttc | ctg | ggg | atc | ttc | ctg | tgc | cct | ctg | tgg  | acg | ctg | 578 |
| Leu | Glu | Thr | Gly | Phe | Leu | Gly | Ile | Phe | Leu | Cys | Pro | Leu | Trp  | Thr | Leu |     |
|     |     |     |     | 175 |     |     |     |     | 180 |     |     |     | ٠    | 185 |     |     |
| tca | agg | ctg | ccc | cag | cat | acc | ccc | aca | tcc | cgg | att | gtc | ctg  | tgg | ggc | 626 |
| Ser | Arg | Leu | Pro | G1n | His | Thr | Pro | Thr | Ser | Arg | Ile | Val | Leu  | Trp | Gly |     |
|     |     |     | 190 |     |     |     |     | 195 |     |     |     |     | 200  |     |     |     |
| ttc | cgg | tgg | ctg | atc | ttc | agg | atc | atg | ctt | gga | gca | ggc | ctg  | atc | aag | 674 |
| Phe | Arg | Trp | Leu | Ile | Phe | Arg | Ile | Met | Leu | Gly | Ala | Gly | Leu  | Ile | Lys |     |
|     |     | 205 |     |     |     |     | 210 |     |     |     |     | 215 |      |     |     |     |
| atc | cgg | ggg | gac | cgg | tgc | tgg | cga | gac | ctc | acc | tgc | atg | gac  | ttc | cac | 722 |
| Ile | Arg | Gly | Asp | Arg | Cys | Trp | Arg | Asp | Leu | Thr | Cys | Met | Asp  | Phe | His |     |
|     | 220 |     |     |     |     | 225 |     |     |     |     | 230 |     |      |     |     |     |
| tat | gag | acc | cag | ccg | atg | ccc | aat | cct | gtg | gca | tac | tac | ctg  | cac | cac | 770 |
|     |     |     |     |     |     |     |     |     |     |     |     |     |      |     |     |     |

| Tyr | Glu | Thr | Gln | Pro | Met | Pro | Asn | Pro | Val | Ala | Tyr | Tyr | Leu | His | His |      |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|------|
| 235 |     |     |     |     | 240 |     |     |     |     | 245 |     |     |     |     | 250 |      |
| tca | ccc | tgg | tgg | ttc | cat | cgc | ttc | gag | acg | ctc | agc | aac | cac | ttc | atc | 818  |
| Ser | Pro | Trp | Trp | Phe | His | Arg | Phe | Glu | Thr | Leu | Ser | Asn | His | Phe | Ile |      |
|     |     |     |     | 255 |     |     |     |     | 260 |     |     |     |     | 265 |     |      |
| gag | ctc | ctg | gtg | ccc | ttc | ttc | ctc | ttc | ctc | ggc | cgg | cgg | gcg | tgc | atc | 866  |
| Glu | Leu | Leu | Val | Pro | Phe | Phe | Leu | Phe | Leu | Gly | Arg | Arg | Ala | Cys | Ile |      |
|     |     |     | 270 |     |     |     |     | 275 |     |     |     |     | 280 |     |     |      |
| atc | cac | ggg | gtg | ctg | cag | atc | ctg | ttc | cag | gcc | gtc | ctc | atc | gtc | agc | 914  |
| Ile | His | Gly | Val | Leu | Gln | Ile | Leu | Phe | Gln | Ala | Val | Leu | Ile | Val | Ser |      |
|     |     | 285 |     |     |     |     | 290 |     |     |     |     | 295 |     |     |     |      |
| gġg | aac | ctc | agc | ttc | ctg | aac | tgg | ctg | act | atg | gtg | ccc | agc | ctg | gcc | 962  |
| G1y | Asn | Leu | Ser | Phe | Leu | Asn | Trp | Leu | Thr | Met | Val | Pro | Ser | Leu | Ala |      |
|     | 300 |     |     |     |     | 305 |     |     |     |     | 310 |     |     |     |     |      |
| tgc | ttt | gat | gac | gcc | acc | ctg | gga | ttc | ttg | ttc | ccc | tct | ggg | cca | ggc | 1010 |
| Cys | Phe | Asp | Asp | Ala | Thr | Leu | Gly | Phe | Leu | Phe | Pro | Ser | Gly | Pro | Gly |      |
| 315 |     |     |     |     | 320 |     |     |     |     | 325 |     |     |     |     | 330 |      |
| agc | ctg | aag | gac | cga | gtt | ctg | cag | atg | cag | agg | gac | atc | cga | ggg | gcc | 1058 |
| Ser | Leu | Lys | Asp | Arg | Val | Leu | Gln | Met | Gln | Arg | Asp | Iļe | Arg | Gly | Ala |      |
|     |     |     |     | 335 |     |     |     |     | 340 |     |     |     |     | 345 |     |      |
| cgg | ccc | gag | ccc | aga | ttc | ggc | tcc | gtg | gtg | cgg | cgt | gca | gcc | aac | gtc | 1106 |
| Arg | Pro | Glu | Pro | Arg | Phe | Gly | Ser | Val | Val | Arg | Arg | Ala | Ala | Asn | Val |      |
|     |     |     | 350 |     |     |     |     | 355 |     |     |     |     | 360 |     |     |      |
| tcg | ctg | ggc | gtc | ctg | ctg | gcc | tgg | ctc | agc | gtg | ccc | gtg | gtc | ctc | aac | 1154 |
| Ser | Leu | Glv | Val | Leu | Leu | Ala | Trp | Leu | Ser | Val | Pro | Val | Val | Leu | Asn |      |

|     |     | 365 |                   |     |     |     | 370 |     |     |     |                  | 375 |     |     |     |      |
|-----|-----|-----|-------------------|-----|-----|-----|-----|-----|-----|-----|------------------|-----|-----|-----|-----|------|
| ttg | ctg | agc | tcc               | agg | cag | gtc | atg | aac | acc | cac | ttc <sub>.</sub> | aac | tct | ctt | cac | 1202 |
| Leu | Leu | Ser | Ser               | Arg | Gln | Val | Met | Asn | Thr | His | Phe              | Asn | Ser | Leu | His |      |
|     | 380 |     |                   |     |     | 385 |     |     |     |     | 390              |     |     |     |     |      |
| atc | gtc | aac | act               | tac | ggg | gcc | ttc | gga | agc | atc | acc              | aag | gag | cgg | gcg | 1250 |
| Ile | Val | Asn | Thr               | Tyr | Gly | Ala | Phe | Gly | Ser | Ile | Thr              | Lys | Glu | Arg | Ala |      |
| 395 |     |     |                   |     | 400 |     |     |     |     | 405 |                  |     |     |     | 410 |      |
| gag | gtg | atc | ctg               | cag | ggc | aca | gcc | agc | tcc | aac | gcc              | agc | gcc | ccc | gat | 1298 |
| Glu | Val | He  | Leu               | Gln | Gly | Thr | Ala | Ser | Ser | Asn | Ala              | Ser | Ala | Pro | Asp |      |
|     |     |     |                   | 415 |     |     |     |     | 420 |     |                  |     |     | 425 |     |      |
| gcc | atg | tgg | gag               | gac | tac | gag | ttc | aag | tgc | aag | cca              | ggt | gac | ccc | agc | 1346 |
| Ala | Met | Trp | G <sub>.</sub> lu | Asp | Tyr | Glu | Phe | Lys | Cys | Lys | Pro              | Gly | Asp | Pro | Ser |      |
|     |     |     | 430               |     |     |     |     | 435 |     |     |                  |     | 440 |     |     |      |
| aga | cgg | ccc | tgc               | ctc | atc | tcc | ccg | tac | cac | tac | cgc              | ctg | gac | tgg | ctg | 1394 |
| Arg | Arg | Pro | Cys               | Leu | Ile | Ser | Pro | Tyr | His | Tyr | Arg              | Leu | Asp | Trp | Leu | •    |
|     |     | 445 |                   |     |     |     | 450 |     |     |     |                  | 455 |     |     |     |      |
| atg | tgg | ttc | gcg               | gcc | ttc | cag | acc | tac | gag | cac | aac              | gac | tgg | atc | atc | 1442 |
| Met | Trp | Phe | Ala               | Ala | Phe | Gln | Thr | Tyr | Glu | His | Asn              | Asp | Trp | Ile | Ile |      |
|     | 460 |     |                   |     |     | 465 |     |     |     |     | 470              |     |     |     |     |      |
| cac | ctg | gct | ggc               | aag | ctc | ctg | gcc | agc | gac | gcc | gag              | gcc | ttg | tcc | ctg | 1490 |
| His | Leu | Ala | Gly               | Lys | Leu | Leu | Ala | Ser | Asp | Ala | Glu              | Ala | Leu | Ser | Leu |      |
| 475 |     |     |                   |     | 480 |     |     |     |     | 485 |                  |     |     |     | 490 |      |
| ctg | gca | cac | aac               | ccc | ttc | gcg | ggc | agg | ccc | ccg | ccc              | agg | tgg | gtc | cga | 1538 |
| Leu | Ala | His | Asn               | Pro | Phe | Ala | Gly | Arg | Pro | Pro | Pro              | Arg | Trp | Val | Arg |      |
|     |     |     |                   | 495 |     |     |     |     | 500 |     |                  |     |     | 505 |     |      |

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| gga gag cac tac agg tac aag | ttc agc cgt cct  | ggg ggc agg cac gcc   | 1586 |
|-----------------------------|------------------|-----------------------|------|
| Gly Glu His Tyr Arg Tyr Lys | Phe Ser Arg Pro  | Gly Gly Arg His Ala   |      |
| 510                         | 515 <sup>-</sup> | 520                   |      |
| gcc gag ggc aag tgg tgg gtg | cgg aag agg atc  | gga gcc tac ttc cct   | 1634 |
| Ala Glu Gly Lys Trp Trp Val | Arg Lys Arg Ile  | Gly Ala Tyr Phe Pro   |      |
| 525                         | 530              | 535                   |      |
| ccg ctc agc ctg gag gag ctg | agg ccc tac ttc  | agg gac cgt ggg tgg   | 1682 |
| Pro Leu Ser Leu Glu Glu Leu | Arg Pro Tyr Phe  | Arg Asp Arg Gly Trp   |      |
| 540 545                     |                  | 550                   |      |
| cct ctg ccc ggg ccc ctc tag | acgtgca ccagaaat | aa aggcgaagac         | 1730 |
| Pro Leu Pro Gly Pro Leu     |                  |                       |      |
| 555 560                     |                  | •                     |      |
| ccagccccc                   |                  |                       | 1739 |
|                             |                  |                       |      |
| <210> 144                   |                  |                       |      |
| <211> 2005                  |                  |                       |      |
| <212> DNA                   |                  |                       |      |
| <213> Homo sapiens          |                  |                       |      |
| <220>                       |                  |                       |      |
| <221> CDS                   |                  |                       |      |
| <222> (107)(1327)           |                  |                       |      |
| <400> 144                   |                  |                       | 1    |
| ggagcccagc ggcgggtgtg agagt | ccgta aggagcagct | tccaggatcc tgagatccgg | 60   |
| agcagccggg gtcggagcgg ctcct | caaga gttactgatc | tatgaa atg gca gag    | 115  |

Met Ala Glu

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1

| aat | gga | aaa | aat | tgt | gac | cag | aga | cgt | gta | gca | atg | aac | aag | gaa | cat |   | 163 |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|---|-----|
| Asn | Gly | Lys | Asn | Cys | Asp | Gln | Arg | Arg | Val | Ala | Met | Asn | Lys | Glu | His | ٠ |     |
|     | 5   |     |     |     |     | 10  |     |     |     |     | 15  |     |     |     |     |   |     |
| cat | aat | gga | aat | ttc | aca | gac | ccc | tct | tca | gtg | aat | gaa | aag | aag | agg |   | 211 |
| His | Asn | Gly | Asn | Phe | Thr | Asp | Pro | Ser | Ser | Val | Asn | Glu | Lys | Lys | Arg |   |     |
| 20  |     |     |     |     | 25  |     |     |     |     | 30  |     |     |     |     | 35  |   |     |
| agg | gag | cgg | gaa | gaa | agg | cag | aat | att | gtc | ctg | tgg | aga | cag | ccg | ctc |   | 259 |
| Arg | Glu | Arg | Glu | Glu | Arg | Gln | Asn | Ile | Val | Leu | Trp | Arg | Gln | Pro | Leu |   |     |
|     |     |     |     | 40  |     |     |     |     | 45  |     |     |     |     | 50  |     |   |     |
| att | acc | ttg | cag | tat | ttt | tct | ctg | gaa | atc | ctt | gta | atc | ttg | aag | gaa |   | 307 |
| Ile | Thr | Leu | Gln | Tyr | Phe | Ser | Leu | Glu | Ile | Leu | Val | Ile | Leu | Lys | Glu |   |     |
|     |     |     | 55  |     |     |     |     | 60  |     |     |     |     | 65  |     |     |   |     |
| tgg | acc | tca | aaa | tta | tgg | cat | cgt | caa | agc | att | gtg | gtg | tct | ttt | tta |   | 355 |
| Trp | Thr | Ser | Lys | Leu | Trp | His | Arg | Gln | Ser | Ile | Val | Val | Ser | Phe | Leu |   |     |
|     |     | 70  |     |     |     |     | 75  |     |     |     |     | 80  |     |     |     |   |     |
| ctg | ctg | ctt | gct | gtg | ctt | ata | gct | acg | tat | tat | gtt | gaa | gga | gtg | cat |   | 403 |
| Leu | Leu | Leu | Ala | Val | Leu | Ile | Ala | Thr | Tyr | Tyr | Val | Glu | Gly | Val | His |   |     |
|     | 85  |     |     |     |     | 90  |     |     |     |     | 95  |     |     |     |     |   |     |
| caa | cag | tat | gtg | caa | cgt | ata | gag | aaa | cag | ttt | ctt | ttg | tat | gcc | tac |   | 451 |
| Gln | Gln | Tyr | Val | Gln | Arg | Ile | Glu | Lys | Gln | Phe | Leu | Leu | Tyr | Ala | Tyr |   |     |
| 100 |     |     |     |     | 105 |     |     |     |     | 110 |     |     |     |     | 115 |   |     |
| tgg | ata | ggc | tta | gga | att | ttg | tct | tct | gtt | ggg | ctt | gga | aca | ggg | ctg |   | 499 |
| Trp | Ile | Gly | Leu | Gly | Ile | Leu | Ser | Ser | Val | Gly | Leu | Gly | Thr | Gly | Leu |   |     |
|     |     |     |     | 120 |     |     |     |     | 125 |     |     |     |     | 130 |     |   |     |

| cac | acc | ttt | ctg | ctt | tat | ctg | ggt | cca | cat | ata | gcc | tca | gtt | aca | tta | 547 |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
| His | Thr | Phe | Leu | Leu | Tyr | Leu | Gly | Pro | His | Ile | Ala | Ser | Val | Thr | Leu |     |
|     |     |     | 135 |     |     |     |     | 140 |     |     |     |     | 145 |     |     |     |
| gct | gct | tat | gaa | tgc | aat | tca | gtt | aat | ttt | ccc | gaa | cca | ccc | tat | cct | 595 |
| Ala | Ala | Tyr | Glu | Cys | Asn | Ser | Val | Asn | Phe | Pro | Glu | Pro | Pro | Tyr | Pro |     |
|     |     | 150 |     |     |     |     | 155 |     |     |     |     | 160 |     |     |     |     |
| gat | cag | att | att | tgt | cca | gat | gaa | gag | ggc | act | gaa | gga | acc | att | tct | 643 |
| Asp | Gln | Ile | Ile | Cys | Pro | Asp | Glu | Glu | Gly | Thr | Glu | Gly | Thr | Ile | Ser |     |
|     | 165 |     |     |     |     | 170 |     |     |     |     | 175 |     |     |     |     |     |
| ttg | tgg | agt | atc | atc | tca | aaa | gtt | agg | att | gaa | gcc | tgc | atg | tgg | ggt | 691 |
| Leu | Trp | Ser | Ile | Ile | Ser | Lys | Val | Arg | Ile | Glu | Ala | Cys | Met | Trp | Gly |     |
| 180 |     |     |     |     | 185 |     |     |     |     | 190 |     |     |     |     | 195 |     |
| atc | ggt | aca | gca | atc | gga | gag | ctg | cct | cca | tat | ttc | atg | gcc | aga | gca | 739 |
| Ile | Gly | Thr | Ala | Ile | Gly | Glu | Leu | Pro | Pro | Tyr | Phe | Met | Ala | Arg | Ala |     |
|     |     |     |     | 200 |     |     |     |     | 205 |     |     |     |     | 210 |     |     |
| gct | cgc | ctc | tca | ggt | gct | gaa | cca | gat | gat | gaa | gag | tat | cag | gaa | ttt | 787 |
| Ala | Arg | Leu | Ser | Gly | Ala | Glu | Pro | Asp | Asp | Glu | Glu | Tyr | Gln | Glu | Phe |     |
|     |     |     | 215 |     |     |     |     | 220 |     |     |     |     | 225 |     |     |     |
| gaa | gag | atg | ctg | gaa | cat | gca | gag | tct | gca | caa | gac | ttt | gcc | tcc | cgg | 835 |
| Glu | Glu | Met | Leu | Glu | His | Ala | Glu | Ser | Ala | Gln | Asp | Phe | Ala | Ser | Arg |     |
|     |     | 230 |     |     |     |     | 235 |     |     |     |     | 240 |     |     |     |     |
| gcc | aaa | ctg | gca | gtt | caa | aaa | cta | gta | cag | aaa | gtt | gga | ttt | ttt | gga | 883 |
| Ala | Lys | Leu | Ala | Val | Gln | Lys | Leu | Val | Gln | Lys | Val | Gly | Phe | Phe | Gly |     |
|     | 245 |     |     |     |     | 250 |     |     |     |     | 255 |     |     |     |     |     |
| att | ttg | gcc | tgt | gct | tca | att | cca | aat | cct | tta | ttt | gat | ctg | gct | gga | 931 |

| Ile | Leu | Ala | Cys | Ala | Ser | Ile | Pro | Asn | Pro | Leu | Phe | Asp | Leu | Ala | Gly |      |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|------|
| 260 |     |     |     |     | 265 |     |     |     |     | 270 |     |     |     |     | 275 | •    |
| ata | acg | tgt | gga | cac | ttt | ctg | gta | cct | ttt | tgg | acc | ttc | ttt | ggt | gca | 979  |
| Ile | Thr | Cys | Gly | His | Phe | Leu | Val | Pro | Phe | Trp | Thr | Phe | Phe | Gly | Ala |      |
|     |     |     |     | 280 |     |     |     |     | 285 |     |     |     |     | 290 |     |      |
| acc | cta | att | gga | aaa | gca | ata | ata | aaa | atg | cat | atc | cag | aaa | att | ttt | 1027 |
| Thr | Leu | Ile | Gly | Lys | Ala | Ile | Ile | Lys | Met | His | Ile | Gln | Lys | Ile | Phe |      |
|     |     |     | 295 |     |     |     |     | 300 |     |     |     |     | 305 |     |     |      |
| gtt | ata | ata | aca | ttc | agc | aag | cac | ata | gtg | gag | caa | atg | gtg | gct | ttc | 1075 |
| Val | Ile | Ile | Thr | Phe | Ser | Lys | His | Ile | Val | Glu | Gln | Met | Val | Ala | Phe |      |
|     |     | 310 |     |     |     |     | 315 |     |     |     |     | 320 |     |     |     |      |
| att | ggt | gct | gtc | ccc | ggc | ata | ggt | cca | tct | ctg | cag | aag | cca | ttt | cag | 1123 |
| Ile | Gly | Ala | Val | Pro | Gly | Ile | Gly | Pro | Ser | Leu | Gln | Lys | Pro | Phe | Gln |      |
|     | 325 |     |     |     |     | 330 |     |     |     |     | 335 |     |     |     |     |      |
| gag | tac | ctg | gag | gct | caa | cgg | cag | aag | ctt | cac | cac | aaa | agc | gaa | atg | 1171 |
| Glu | Tyr | Leu | Glu | Ala | Gln | Arg | Gln | Lys | Leu | His | His | Lys | Ser | Glu | Met |      |
| 340 |     |     |     |     | 345 |     |     |     |     | 350 |     |     |     |     | 355 |      |
| ggc | aca | cca | cag | gga | gaa | aac | tgg | ttg | tcc | tgg | atg | ttt | gaa | aag | ttg | 1219 |
| Gly | Thr | Pro | Gln | Gly | Glu | Asn | Trp | Leu | Ser | Trp | Met | Phe | Glu | Lys | Leu |      |
|     |     |     |     | 360 |     |     |     |     | 365 |     |     |     |     | 370 |     |      |
| gtc | gtt | gtc | atg | gtg | tgt | tac | ttc | atc | cta | tct | atc | att | aac | tcc | atg | 1267 |
| Val | Val | Val | Met | Val | Cys | Tyr | Phe | Ile | Leu | Ser | Ile | Ile | Asn | Ser | Met |      |
|     |     |     | 375 |     |     |     |     | 380 |     |     |     |     | 385 |     |     |      |
| gca | caa | agt | tat | gcc | aaa | cga | atc | cag | cag | cgg | ttg | aac | tca | gag | gag | 1315 |
| Ala | Gln | Ser | Tyr | Ala | Lys | Arg | Ile | Gln | Gln | Arg | Leu | Asn | Ser | Glu | Glu |      |

390 395 400 aaa act aaa taagta gagaaagttt taaactgcag aaattggagt ggatgggttc 1370 Lys Thr Lys 405 tgccttaaat tgggaggact ccaagccggg aaggaaaatt cccttttcca acctgtatca 1430 attittacaa ciiitticci gaaagcagii tagiccatac tiigcaciga cataciitti 1490 ccttctgtgc taaggtaagg tatccaccct cgatgcaatc caccttgtgt tttcttaggg 1550 tggaatgtga tgttcagcag caaacttgca acagactggc cttctgtttg ttactttcaa 1610 aaggcccaca tgatacaatt agagaattcc caccgcacaa aaaaagttcc taagtatgtt 1670 aaatatgtca agctttttag gcttgtcaca aatgattgct ttgttttcct aagtcatcaa 1730 aatgtatata aattatctag attggataac agtcttgcat gtttatcatg ttacaattta 1790 atattccatc ctgcccaacc cttcctctc catcctcaaa aaagggccat tttatgatgc 1850 attgcacacc ctctggggaa attgatcttt aaattttgag acagtataag gaaaatctgg 1910 ttggtgtctt acaagtgagc tgacaccatt ttttattctg tgtatttaga atgaagtctt 1970 gaaaaaaact ttataaagac atctttaatc attcc 2005

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<220>

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WO 01/12660 PCT/JP00/05356

#### 294/307

Met Gly Val Leu Gly Arg Val Leu

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|     |     |     |     | 125 |     |     |     |     | 130 |     |     |     |     | 135 |     |     |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
| tgc | cgc | cac | gac | gac | gtc | ttc | ttt | ccg | cct | agt | gcc | tcc | ttc | cgc | gtg | 486 |
| Cys | Arg | His | Asp | Asp | Val | Phe | Phe | Pro | Pro | Ser | Ala | Ser | Phe | Arg | Val |     |
|     |     |     | 140 |     |     |     |     | 145 |     |     |     |     | 150 |     |     |     |
| ggg | ctc | ggc | cct | ggc | gct | agc | ccc | gtg | cgt | gtc | cgc | agc | atc | tcg | gct | 534 |
| Gly | Leu | Gly | Pro | Gly | Ala | Ser | Pro | Val | Arg | Val | Arg | Ser | Ile | Ser | Ala |     |
|     |     | 155 |     |     |     |     | 160 |     |     |     |     | 165 | •   |     |     |     |
| ctg | ggc | cgg | acg | ttc | acg | cgc | gac | gag | gac | ctg | gct | gtt | ttc | ctg | gcg | 582 |
| Leu | Gly | Arg | Thr | Phe | Thr | Arg | Asp | Glu | Asp | Leu | Ala | Val | Phe | Leu | Ala |     |
|     | 170 |     |     |     |     | 175 |     |     |     |     | 180 |     |     |     |     |     |
| tcc | cgc | gcg | ggc | cgc | cta | cgc | ttc | cac | ggg | ccg | ggc | gcg | ctg | agc | gtg | 630 |
| Ser | Arg | Ala | Gly | Arg | Leu | Arg | Phe | His | Gly | Pro | Gly | Ala | Leu | Ser | Val |     |
| 185 |     |     |     |     | 190 |     |     |     |     | 195 |     |     |     |     | 200 |     |
| ggc | ccc | gag | gac | tgc | gcg | gac | ccg | tcg | ggc | tgc | gtc | tgc | ggc | aac | gcg | 678 |
| Gly | Pro | Glu | Asp | Cys | Ala | Asp | Pro | Ser | Gly | Cys | Val | Cys | Gly | Asn | Ala |     |
|     |     |     |     | 205 |     |     |     |     | 210 |     |     |     |     | 215 |     |     |
| gag | gcg | cag | ccg | tgg | atc | tgc | gcg | gcc | ctg | ctc | cag | ccc | ctg | ggc | ggc | 726 |
| Glu | Ala | Gln | Pro | Trp | Ile | Cys | Ala | Ala | Leu | Leu | Gln | Pro | Leu | Gly | Gly |     |
|     |     |     | 220 |     |     |     |     | 225 |     |     |     |     | 230 |     |     |     |
| cgc | tgc | ccc | cag | gcc | gcc | tgc | cac | agc | gcc | ctc | cgg | ccc | cag | ggg | cag | 774 |
| Arg | Cys | Pro | Gln | Ala | Ala | Cys | His | Ser | Ala | Leu | Arg | Pro | Gln | Gly | G1n |     |
|     |     | 235 |     |     |     |     | 240 |     |     |     |     | 245 |     |     |     |     |
| tgc | tgt | gac | ctc | tgt | gga | gcc | gtt | gtg | ttg | ctg | acc | cac | ggc | ссс | gca | 822 |
| Cys | Cys | Asp | Leu | Cys | Gly | Ala | Val | Val | Leu | Leu | Thr | His | Gly | Pro | Ala |     |
|     | 250 |     |     |     |     | 255 |     |     |     |     | 260 |     |     |     |     |     |

| 870  | ggt | ctg | ttc | acc | gac | ctg | ata | cgg | gcg | cgg | tac | cgg | gag | ctg | gac | ttt |
|------|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
|      | Gly | Leu | Phe | Thr | Asp | Leu | Ile | Arg | Ala | Arg | Tyr | Arg | Glu | Leu | Asp | Phe |
|      | 280 |     |     |     |     | 275 |     |     | ÷   |     | 270 |     |     |     |     | 265 |
| 918  | cgc | cca | gtg | aag | tcc | gtg | gcc | gtg | cag | ctg | ggg | cac | tac | cag | cct | ctg |
|      | Arg | Pro | Val | Lys | Ser | Val | Ala | Val | Gln | Leu | Gly | His | Tyr | G1n | Pro | Leu |
|      |     | 295 |     |     |     |     | 290 |     |     |     |     | 285 |     |     |     |     |
| 966  | gtg | ctg | gtg | gtg | cag | atc | gag | acg | gat | gcc | gag | cgt | ctc | cgg | tcc | tcg |
|      | Val | Leu | Val | Val | Gln | Ile | Glu | Thr | Asp | Ala | Glu | Arg | Leu | Arg | Ser | Ser |
|      |     |     | 310 |     |     |     |     | 305 |     |     |     |     | 300 |     |     |     |
| 1014 | ctc | gcc | cgg | gcc | ctg | cgg | ggg | gcg | gga | ggc | aca | gag | ccc | ggg | aat | gag |
|      | Leu | Ala | Arg | Ala | Leu | Arg | Gly | Ala | Gly | Gly | Thr | Glu | Pro | Gly | Asn | Glu |
|      |     |     |     | 325 |     |     |     |     | 320 |     |     |     |     | 315 |     |     |
| 1062 | gcg | gag | ctg | gtc | ggc | ctc | gcc | gag | ggc | aac | gag | gcc | gtc | gac | gcg | ctg |
|      | Ala | Glu | Leu | Val | Gly | Leu | Ala | Glu | Gly | Asn | Glu | Ala | Val | Asp | Ala | Leu |
|      |     |     |     |     | 340 |     |     |     |     | 335 |     |     |     |     | 330 |     |
| 1110 | ggg | gct | gcg | tcc | agc | ggc | tgg | gtc | cac | gca | ggc | tcg | gag | cgg | atg | acc |
|      | Gly | Ala | Ala | Ser | Ser | Gly | Trp | Val | His | Ala | Gly | Ser | Glu | Arg | Met | Thr |
|      | 360 |     |     |     |     | 355 |     |     |     |     | 350 |     |     |     |     | 345 |
| 1158 | ctg | gtc | ctg | ctg | gcg | ctg | ctg | gtg | gcc | gct | gcg | gtg | ggc | ggc | gcg | ctg |
|      | Leu | Val | Leu | Leu | Ala | Leu | Leu | Val | Ala | Ala | Ala | Val | Gly | Gly | Ala | Leu |
|      |     | 375 |     |     |     |     | 370 |     |     |     |     | 365 |     |     |     |     |
| 1206 | agg | tgg | agg | ctc | agg | ggg | gcg | cgc | cgc | ctg | ctg | ccg | ccg | gcg | gtg | ctg |
|      | Arg | Trp | Arg | Leu | Arg | Gly | Ala | Arg | Arg | Leu | Leu | Pro | Pro | Ala | Val | Leu |
|      |     |     | 390 |     |     | -   |     | 385 |     |     |     |     | 380 |     |     |     |
| 1254 | aac | cgc | ttc | ggc | ctc | ccc | gcg | gga | gct | ccg | gcc | gcg | gcg | gag | cac | agg |

| Arg His Glu | u Ala Ala Ala | Pro Ala Gly   | Ala Pro Leu  | ı Gly Phe Arg Asn  |      |
|-------------|---------------|---------------|--------------|--------------------|------|
| 398         | 5             | 400           |              | 405                |      |
| ccg gtg tto | c gac gtg acg | gcc tcc gag   | gag ctg ccc  | ctg ccg cgg cgg    | 1302 |
| Pro Val Phe | e Asp Val Thr | Ala Ser Glu   | Glu Leu Pro  | Leu Pro Arg Arg    |      |
| 410         |               | 415           | 420          | )                  |      |
| ctc agc ctg | g gtt ccg aag | gcg gcc gca   | gac agc acc  | agc cac agt tac    | 1350 |
| Leu Ser Leu | ı Val Pro Lys | Ala Ala Ala   | Asp Ser Thr  | Ser His Ser Tyr    |      |
| 425         | 430           |               | 435          | 440                |      |
| ttc gtc aac | cct ctg ttc   | gcc ggg gcc   | gag gcc gag  | gcc t gagcggccgc   | 1400 |
| Phe Val Asn | n Pro Leu Phe | Ala Gly Ala   | Glu Ala Glu  | Ala                | C    |
|             | 445           |               | 450          |                    |      |
| ctgaccgtcg  | accttggggc to | ctccacccc ctc | etggcccc agt | cgaactg ggggctagcc | 1460 |
| acctcctcgt  | ccagccccca a  | aceteceet tee | tttcccc ctc  | ctccggg ggccaaggac | 1520 |
| agggtggcct  | tactcagtaa a  | ggtgtttcc tgc | acctg        |                    | 1558 |
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| <211> 1005  |               |               |              |                    |      |
| <212> DNA   |               |               |              |                    |      |
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| <222> (151) | (330)         |               |              |                    |      |
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| attcctgtaa  | tggctgcttc ct | agaaggtc gtg  | tcacgtg gaad | ectetta ateteageat | 60   |
|             |               |               |              |                    |      |

ccggagctcc aggaagggaa aatttcaagt cagatagaat tctatatata ccatttcttt 120

| ggaacettea geeeteaaga tteeaacate atg ace tea gt | t tca aca cag ttg 174  |
|---|------------------------|
| Met Thr Ser Va                                  | l Ser Thr Gln Leu      |
| 1   | 5                      |
| tcc tta gtc ctc atg tca ctg ctt ttg gtg ctg cct | gtt gtg gaa gca 222    |
| Ser Leu Val Leu Met Ser Leu Leu Leu Val Leu Pro | Val Val Glu Ala        |
| 10 15 20  |                        |
| gta gaa gcc ggt gat gca atc gcc ctt ttg tta ggt | gtg gtt ctc agc 270    |
| Val Glu Ala Gly Asp Ala Ile Ala Leu Leu Leu Gly | Val Val Leu Ser        |
| 25 30 35  | 40                     |
| att aca ggc att tgt gcc tgc ttg ggg gta tat gca | cga aaa aga aat 318    |
| Ile Thr Gly Ile Cys Ala Cys Leu Gly Val Tyr Ala | Arg Lys Arg Asn        |
| 45 50   | 55                     |
| gga cag atg tga ctttgaaagg cctactgagt caaacctca | c cctgaaaacc 370       |
| Gly Gln Met                                     |                        |
| tttgcgcttt agaggctaaa cctgagattt ggtgtgtgaa agg | ttccaag aatcagtaaa 430 |
| taagggagtt teacattttt cattgtttee atgaaatgge aac | aaacata catttataaa 490 |
| ttgaaaaaaa aatgttttct ttacaacaaa taatgcacag aaa | aatgcag cctataattt 550 |
| gctagttagg tagtcaaaga agtaagatgg ctgaaattta cat | aagtaat atttcataat 610 |
| cttagaattc tctcaaagca tgtgaaatag gaagaaggaa gtt | cttgccc agaatcttag 670 |
| gaaatcacca ctgttcggtt ataatcactg cctcctgaat cgt | tgaggag tcttttaaat 730 |
| tagatttttg ttttgttgtc tcccaagtta atattatatt     | atatcag agagtcaggc 790 |
| aaaaaggaaa acttttatct ctagggaaaa aacatttaga aaa | atgtatt cagtgtatct 850 |
| aatactgaaa tgcggaaaaa aatttaatgt taaaaaaaaa act | atagaca ttgacatgga 910 |
| aaagagattt aatgttttga aaaaaaactt tatattaact gag | taacatc ctcctgatga 970 |
| gaagtactat attaaatata aacccattat gttat          | 1005                   |

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| <22 | 2> (  | 151) | (    | 783) |      |      |      |      |       |      |       |       |      |      |        |       |
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| gct | ggac  | acc  | tgga | gctg | cc c | gagg | acgc | g ga | ggag  | agac | ccg   | aggg  | tcg  | ccgc | tggtag | g 60  |
| ggt | cgct  | cag  | ccct | gccg | tc c | ttca | ccac | c ac | acct  | tcac | ctg   | egec  | cag  | ctcc | ctgcgc | : 120 |
| gcc | tgga  | cag  | cgcc | tgct | gc c | cgcc | tccc | g at | g gc  | c ct | g cc  | cca   | g at | g tg | t gac  | 174   |
|     |       |      |      |      |      |      |      | Me   | t Ala | a Le | u Pro | o Gli | n Me | t Cy | s Asp  | •     |
|     |       |      |      |      |      |      |      |      | 1     |      |       | !     | 5    |      |        |       |
| ggg | agc   | cac  | ttg  | gcc  | tcc  | acc  | ctc  | cgc  | tat   | tgc  | atg   | aca   | gtc  | agc  | ggc    | 222   |
| Gly | Ser   | His  | Leu  | Ala  | Ser  | Thr  | Leu  | Arg  | Tyr   | Cys  | Met   | Thr   | Val  | Ser  | Gly    |       |
|     | 10    |      |      |      |      | 15   |      |      |       |      | 20    |       |      |      |        |       |
| aca | gtg   | gtt  | ctg  | gtg  | gcc  | ggg  | acg  | ctc  | tgc   | ttc  | gct   | tgg   | tgg  | agc  | gaa    | 270   |
| Thr | Val   | Val  | Leu  | Val  | Àla  | Gly  | Thr  | Leu  | Cys   | Phe  | Ala   | Trp   | Trp  | Ser  | Glu    |       |
| 25  |       |      |      |      | 30   |      |      |      |       | 35   |       |       |      |      | 40     |       |
| ggg | gat   | gca  | acc  | gcc  | cag  | cct  | ggc  | cag  | ctg   | gcc  | cca   | ccc   | acg  | gag  | tat    | 318   |
| Gly | Asp   | Ala  | Thr  | Ala  | Gln  | Pro  | Gly  | Gln  | Leu   | Ala  | Pro   | Pro   | Thr  | Glu  | Tyr    |       |
|     |       |      |      | 45   |      |      |      |      | 50    |      |       |       |      | 55   |        |       |
| ccg | gtg   | cct  | gag  | ggc  | ccc  | agc  | ccc  | ctg  | ctc   | agg  | tcc   | gtc   | agc  | ttc  | gtc    | 366   |
| Pro | Val   | Pro  | Glu  | Glv  | Pro  | Sor  | Pro  | Lau  | Lou   | Ara  | San   | Vo 1  | Sor  | Pho  | Val    |       |

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|     |     |     | 60  |     |     |     |     | 65  |     |     |     |     | 70  |     |     |            |     |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|------------|-----|
| tgc | tgc | ggt | gca | ggt | ggc | ctg | ctg | ctg | ctc | att | ggc | ctg | ctg | tgg | tcc | 4          | 414 |
| Cys | Cys | Gly | Ala | Gly | Gly | Leu | Leu | Leu | Leu | Ile | Gly | Leu | Leu | Trp | Ser |            |     |
|     |     | 75  |     |     |     |     | 80  |     |     |     |     | 85  |     |     |     |            |     |
| gtc | aag | gcc | agc | atc | cca | ggg | cca | cct | cga | tgg | gac | ccc | tat | cac | ctc | 4          | 462 |
| Val | Lys | Ala | Ser | Ile | Pro | Gly | Pro | Pro | Arg | Trp | Asp | Pro | Tyr | His | Leu |            |     |
|     | 90  |     |     |     |     | 95  |     |     |     |     | 100 |     |     |     |     |            |     |
| tcc | aga | gac | ctg | tac | tac | ctc | act | gtg | gag | tcc | tca | gag | aag | gag | agc | (          | 510 |
| Ser | Arg | Asp | Leu | Tyr | Tyr | Leu | Thr | Val | Glu | Ser | Ser | Glu | Lys | Glu | Ser |            |     |
| 105 |     |     |     |     | 110 |     |     |     |     | 115 |     |     |     |     | 120 |            |     |
| tgc | agg | acc | ccc | aaa | gtg | gtt | gac | atc | ccc | act | tac | gag | gaa | gcc | gtg | 5          | 558 |
| Cys | Arg | Thr | Pro | Lys | Val | Val | Asp | Ile | Pro | Thr | Tyr | Glu | Glu | Ala | Val |            |     |
|     |     |     |     | 125 |     |     |     |     | 130 |     |     |     |     | 135 |     |            |     |
| agc | ttc | cca | gtg | gcc | gag | ggg | ccc | cca | aca | cca | cct | gca | tac | cct | acg | $\epsilon$ | 606 |
| Ser | Phe | Pro | Val | Ala | Glu | Gly | Pro | Pro | Thr | Pro | Pro | Ala | Tyr | Pro | Thr |            |     |
|     |     |     | 140 |     |     |     |     | 145 |     |     |     |     | 150 |     |     |            |     |
| gag | gaa | gcc | ctg | gag | cca | agt | gga | tcg | agg | gat | gcc | ctg | ctc | agc | acc | 6          | 554 |
| Glu | Glu | Ala | Leu | Glu | Pro | Ser | Gly | Ser | Arg | Asp | Ala | Leu | Leu | Ser | Thr |            |     |
|     |     | 155 |     |     |     |     | 160 |     |     |     |     | 165 |     |     |     |            |     |
| cag | ccc | gcc | tgg | cct | cca | ccc | agc | tat | gag | agc | atc | agc | ctt | gct | ctt | 7          | '02 |
| Gln | Pro | Ala | Trp | Pro | Pro | Pro | Ser | Tyr | Glu | Ser | Ile | Ser | Leu | Ala | Leu |            |     |
|     | 170 |     |     |     |     | 175 |     |     |     |     | 180 |     |     |     |     |            |     |
| gat | gcc | gtt | tct | gca | gag | acg | aca | ccg | agt | gcc | aca | cgc | tcc | tgc | tca | 7          | '50 |
| Asp | Ala | Val | Ser | Ala | Glu | Thr | Thr | Pro | Ser | Ala | Thr | Arg | Ser | Cys | Ser |            |     |
| 185 |     |     |     |     | 190 |     |     |     |     | 195 |     |     |     |     | 200 |            |     |

| ggc ctg gtt cag act gca cgg gga gga agt taaaggctcc tagcaggtcc     | 800 |
|---|-----|
| Gly Leu Val Gln Thr Ala Arg Gly Gly Ser                           |     |
| 205 210   |     |
| tgaatccaga gacaaaaatg ctgtgccttc tccagagtct tatgcagtgc ctgggacaca | 860 |
| gtaggcactc agcaaacgtt cgttgttgaa ggctgttcta tttatctatt gctgtataac | 920 |
| aaaccacccc agaatttagt ggcttaaaat aaatcccatt ttattatgt             | 969 |
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| atttcggggc ggtaccaag atg gac tcc tcg cgg gcc cga cag cag ctc cgg  | 52  |
| Met Asp Ser Ser Arg Ala Arg Gln Gln Leu Arg                       |     |
| 1 5 10  |     |
| cgg cga ttc ctc ctg ccg gac gcc gag gcc cag ctg gac cgc gag       | 100 |
| Arg Arg Phe Leu Leu Pro Asp Ala Glu Ala Gln Leu Asp Arg Glu       |     |
| 15 20 25  |     |
| ggt gac gcc ggg ccg gaa acc tcc aca gct gtt gag aaa aag gag aaa   | 148 |
| Gly Asp Ala Gly Pro Glu Thr Ser Thr Ala Val Glu Lys Lys Glu Lys   |     |
| 30 35 40  |     |
| cct ctt cca aga ctt aat atc cat tct gga ttc tgg att ttg gca tcc   | 196 |

|      | 45    |      |       |       |       | 50    |       |     |      |      | 55   |       |       |       |        |     |
|------|-------|------|-------|-------|-------|-------|-------|-----|------|------|------|-------|-------|-------|--------|-----|
|      |       |      |       |       |       |       |       |     |      |      |      |       |       |       |        |     |
| att  | gtt   | gtg  | acc   | tat   | tat   | gtt   | gac   | ttc | ttt  | aaa  | acc  | ctt   | aaa   | gaa   | aac    | 244 |
| Ile  | Val   | Val  | Thr   | Tyr   | Tyr   | Val   | Asp   | Phe | Phe  | Lys  | Thr  | Leu   | Lys   | Glu   | Asn    |     |
| 60   |       |      |       |       | 65    |       |       |     |      | 70   |      |       |       |       | 75     |     |
| ttc  | cac   | act  | agc   | agc   | tgg   | ttt   | ctc   | tgt | ggc  | agt  | gcc  | ttg   | ttg   | ctt   | gtc    | 292 |
| Phe  | His   | Thr  | Ser   | Ser   | Trp   | Phe   | Leu   | Cys | Gly  | Ser  | Ala  | Leu   | Leu   | Leu   | Val    |     |
|      |       |      |       | 80    |       |       |       |     | 85   |      |      |       |       | 90    |        |     |
| agt  | tta   | tca  | att   | gca   | ttt   | tac   | tgc   | ata | gtc  | tac  | ctg  | gaa   | tgg   | tat   | tgt    | 340 |
| Ser  | Leu   | Ser  | Ile   | Ala   | Phe   | Tyr   | Cys   | Ile | Val  | Tyr  | Leu  | Glu   | Trp   | Tyr   | Cys    |     |
|      |       |      | 95    |       |       |       |       | 100 |      |      |      |       | 105   |       |        | 4   |
| gga  | att   | gga  | gaa   | tat   | gat   | gtc   | aag   | tat | cca  | gcc  | ttg  | ata   | ccc   | att   | acc    | 388 |
| Gly  | Ile   | Gly  | Glu   | Tyr   | Asp   | Val   | Lys   | Tyr | Pro  | Ala  | Leu  | Ile   | Pro   | Ile   | Thr    |     |
|      |       | 110  |       |       |       |       | 115   |     |      |      |      | 120   |       |       |        |     |
| act  | gcc   | tcc  | ttt   | att   | gca   | gca   | gga   | att | tgc  | ttc  | aac  | att   | gct   | tta   | tgg    | 436 |
| Thr  | Ala   | Ser  | Phe   | Ile   | Ala   | Ala   | Gly   | Ile | Cys  | Phe  | Asn  | Ile   | Ala   | Leu   | Trp    |     |
|      | 125   |      |       |       |       | 130   |       |     |      |      | 135  |       |       |       |        |     |
| cat  | gtg   | tgg  | tcg   | ttt   | ttc   | act   | cca   | ttg | ttg  | ttg  | ttt  | acc   | cag   | ttt   | atg    | 484 |
| His  | Val   | Trp  | Ser   | Phe   | Phe   | Thr   | Pro   | Leu | Leu  | Leu  | Phe  | Thr   | Gln   | Phe   | Met    |     |
| 140  |       |      |       |       | 145   |       |       |     |      | 150  |      |       |       |       | 155    |     |
| ggg  | gtt   | gtc  | atg   | ttt   | atc   | aca   | ctc   | ctt | gga  | tgat | tt d | cgaa  | agaga | ac    |        | 530 |
| Gly  | Val   | Val  | Met   | Phe   | Ile   | Thr   | Leu   | Leu | Gly  |      |      |       |       |       |        |     |
|      |       |      |       | 160   |       |       |       |     | 165  |      |      |       |       |       |        |     |
| aggg | gtcti | ct a | atgtt | gcc   | ca gg | gctgi | tctt1 | gaa | ctco | tgg  | gato | caagt | tga t | tecto | ectged | 590 |
| tcag | ccti  | cg a | aagta | ngtte | gg ga | acta  | caggo | cca | cgc  | acc  | gtgo | ctg   | gct g | ggaca | atgtaa | 650 |

| aaaa 710  | taacagaaa | tggcagaccc | gctgaaagca | catccagcta | aatggttaaa | atttgaagtg |
|-----------|-----------|------------|------------|------------|------------|------------|
| tttg 770  | tgtgactti | tggggaaaat | aatggtttcc | ctatgaagtg | gtttttgcag | gctacagtgt |
| ttaa 830  | aaattatta | gcatatgcat | tatttcactt | gaataaatta | gttgaaacca | tataactgtt |
| tctt 890  | tttgagtc  | tgttaatctg | tattttgcaa | acagaagtac | agtcagtgat | aattttcaga |
| agtt 950  | acaagtagt | aatatttaa  | gtgcactgtt | taggtacata | ggtttcattg | tggagaaagt |
| agga 1010 | gtataaagg | gactggatgt | tgtataaaat | agcagttcct | tttaagggat | cactcttcca |
| tgat 1070 | tatttatga | tataatctca | tagtaattac | taaccagctt | catgtgcctt | attatgttgt |
| gatt 1130 | actttagat | ttttctcatc | atattttatg | ccaaatgaaa | ggtgacagga | agttttgtta |
| cttt 1190 | taatcacti | tgtgaagttt | catttcctaa | gggtttttag | gtacattact | ttatcattat |
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cagccaggag cggtttctg ggaactgtgg gatgtgccct tgggggcccg agaaaacaga 180
aggaag atg ctc cag acc agt aac tac agc ctg gtg ctc tct ctg cag 228

Met Leu Gln Thr Ser Asn Tyr Ser Leu Val Leu Ser Leu Gln

10

5

| ttc | ctg | ctg | ctg | tcc | tat | gac | ctc | ttt | gtc | aat | tcc | ttc | tca | gaa | ctg | 276 |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
| Phe | Leu | Leu | Leu | Ser | Tyr | Asp | Leu | Phe | Val | Asn | Ser | Phe | Ser | Glu | Leu |     |
| 15  |     |     | ٠   |     | 20  |     |     |     |     | 25  |     |     |     |     | 30  |     |
| ctc | caa | aag | act | cct | gtc | atc | cag | ctt | gtg | ctc | ttc | atc | atc | cag | gat | 324 |
| Leu | Gln | Lys | Thr | Pro | Val | Ile | Gln | Leu | Val | Leu | Phe | Ile | Ile | Gln | Asp |     |
|     |     |     |     | 35  |     |     |     |     | 40  |     |     |     |     | 45  |     |     |
| att | gca | gtc | ctc | ttc | aac | atc | atc | atc | att | ttc | ctc | atg | ttc | ttc | aac | 372 |
| Ile | Ala | Val | Leu | Phe | Asn | Ile | Ile | Ile | Ile | Phe | Leu | Met | Phe | Phe | Asn |     |
|     |     |     | 50  |     |     |     |     | 55  |     |     |     |     | 60  |     |     |     |
| acc | ttc | gtc | ttc | cag | gct | ggc | ctg | gtc | aac | ctc | cta | ttc | cat | aag | ttc | 420 |
| Thr | Phe | Val | Phe | Gln | Ala | Gly | Leu | Val | Asn | Leu | Leu | Phe | His | Lys | Phe |     |
|     |     | 65  |     |     |     |     | 70  |     |     |     |     | 75  |     |     |     |     |
| aaa | ggg | acc | atc | atc | ctg | aca | gct | gtg | tac | ttt | gcc | ctc | agc | atc | tcc | 468 |
| Lys | Gly | Thr | Ile | Ile | Leu | Thr | Ala | Val | Tyr | Phe | Ala | Leu | Ser | Ile | Ser |     |
|     | 80  |     |     |     |     | 85  |     |     |     |     | 90  |     |     |     |     |     |
| ctt | cat | gtc | tgg | gtc | atg | aac | tta | cgc | tgg | aaa | aac | tcc | aac | agc | ttc | 516 |
| Leu | His | Val | Trp | Val | Met | Asn | Leu | Arg | Trp | Lys | Asn | Ser | Asn | Ser | Phe |     |
| 95  |     |     |     |     | 100 |     |     |     |     | 105 |     |     |     |     | 110 |     |
| ata | tgg | aca | gat | gga | ctt | caa | atg | ctg | ttt | gta | ttc | cag | aga | cta | gca | 564 |
| Ile | Trp | Thr | Asp | Gly | Leu | G1n | Met | Leu | Phe | Val | Phe | Gln | Arg | Leu | Ala |     |
|     |     |     |     | 115 |     |     |     |     | 120 |     |     |     |     | 125 |     |     |
| gca | gtg | ttg | tac | tgc | tac | ttc | tat | aaa | cgg | aca | gcc | gta | aga | cta | ggc | 612 |
| Ala | Val | Leu | Tyr | Cys | Tyr | Phe | Tyr | Lys | Arg | Thr | Ala | Val | Arg | Leu | Gly |     |
|     |     |     | 130 |     |     |     |     | 135 |     |     |     |     | 140 |     |     |     |
| gat | cct | cac | ttc | tac | cag | gac | tct | ttg | tgg | ctg | cgc | aag | gag | ttc | atg | 660 |

Asp Pro His Phe Tyr Gln Asp Ser Leu Trp Leu Arg Lys Glu Phe Met

145 150 155

caa gtt cga agg tgacctct tgtcacactg atggatactt ttccttcctg 710
Gln Val Arg Arg

160

770 atagaagcca catttgctgc tttgcaggga gagttggccc tatgcatggg caaacagctg 830 gactttccaa ggaaggttca gactagctgt gttcagcatt caagaaggaa gatcctccct 890 cttgcacaat tagagtgtcc ccatcggtct ccagtgcggc atcccttcct tgccttctac 950 ctctgttcca ccccctttcc ttcctttcct ctctgtacca ttcattctcc ctgaccggcc tttcttgccg agggttctgt ggctcttacc cttgtgaagc ttttccttta gcctgggaca 1010 1070 gaaggacctc ccagccccca aaggatctcc cagtgaccaa aggatgcgaa gagtgatagt 1130 tacgtgctcc tgactgatca caccgcagac atttagattt ttatacccaa ggcactttaa 1174 aaaaatgttt tataaataga gaataaattg aattcttgtt ccat

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eggeeteea gegeteeaa geegeagegg eegegeeet teagetaget egetegeteg 180

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| ctct | gctt | cc ( | ctgct | gccg | gg ct | gcgc | c at | tg go | g ti  | tg go | g tt  | g g      | cg go | cg c1 | tg   | 231 |
|------|------|------|-------|------|-------|------|------|-------|-------|-------|-------|----------|-------|-------|------|-----|
|      |      |      |       |      |       |      | Ме   | et Al | la Le | eu Al | la Le | eu A     | la Al | la Ļ  | eu į |     |
|      |      |      |       |      |       |      |      | 1     |       |       |       | 5        |       |       |      |     |
| gcg  | gcg  | gtc  | gag   | ccg  | gcc   | tgc  | ggc  | agc   | cgg   | tac   | cag   | cag      | ttg   | cag   | aat  | 279 |
| Ala  | Ala  | Val  | Glu   | Pro  | Ala   | Cys  | Gly  | Ser   | Arg   | Tyr   | Gln   | Gln      | Leu   | G1n   | Asn  |     |
|      | 10   |      |       |      |       | 15   |      |       |       |       | 20    |          |       |       |      |     |
| gaa  | gaa  | gag  | tct   | gga  | gaa   | cct  | gaa  | cag   | gct   | gca   | ggt   | gat      | gct   | cct   | cca  | 327 |
| Glu  | Glu  | Glu  | Ser   | Gly  | Glu   | Pro  | Glu  | Gln   | Ala   | Ala   | Gly   | Asp      | Ala   | Pro   | Pro  |     |
| 25   |      |      |       |      | 30    |      |      |       |       | 35    |       |          |       |       | 40   |     |
| cct  | tac  | agc  | agc   | att  | tct   | gca  | gag  | agc   | gca   | gca   | tat   | ttt      | gac   | tac   | aag  | 375 |
| Pro  | Tyr  | Ser  | Ser   | Ile  | Ser   | Ala  | Glu  | Ser   | Ala   | Ala   | Tyr   | Phe      | Asp   | Tyr   | Lys  |     |
|      |      |      | •     | 45   |       |      |      |       | 50    |       |       |          |       | 55    |      |     |
| gat  | gag  | tct  | ggg   | ttt  | cca   | aag  | ссс  | cca   | tct   | tac   | aat   | gta      | gct   | aca   | aca  | 423 |
| Asp  | Glu  | Ser  | Gly   | Phe  | Pro   | Lys  | Pro  | Pro   | Ser   | Tyr   | Asn   | Val      | Ala   | Thr   | Thr  |     |
|      |      |      | 60    |      |       |      |      | 65    |       |       |       |          | 70    |       |      |     |
| ctg  | ссс  | agt  | tat   | gat  | gaa   | gcg  | gag  | agg   | acc   | aag   | gct   | gaa      | gct   | act   | atc  | 471 |
| Leu  | Pro  | Ser  | Tyr   | Asp  | Glu   | Ala  | Glu  | Arg   | Thr   | Lys   | Ala   | Glu      | Ala   | Thr   | Ile  |     |
|      |      | 75   |       |      |       |      | 80   |       |       |       |       | 85       |       |       |      |     |
| cct  | ttg  | gtt  | cct   | ggg  | aga   | gat  | gag  | gat   | ttt   | gtg   | ggt   | cgg      | gat   | gat   | ttt  | 519 |
| Pro  | Leu  | Val  | Pro   | Gly  | Arg   | Asp  | Glu  | Asp   | Phe   | Val   | Gly   | Arg      | Asp   | Asp   | Phe  |     |
|      | 90   |      |       |      |       | 95   |      |       |       |       | 100   |          |       |       |      |     |
| gat  | gat  | gct  | gac   | cag  | ctg   | agg  | ata  | gga   | aat   | gat   |       | att      | ttc   | atg   | tta  | 567 |
|      |      |      | Asp   |      |       |      |      |       |       |       |       |          |       |       |      |     |
| 105  | •    |      | - 4   |      | 110   | 3    |      | -,    |       | 115   | /     |          |       | - *   | 120  |     |
|      | ttt  | ttc  | atg   | gca  |       | ete  | +++  | aac   | taa   |       | aaa   | <b>t</b> | ttc   | ctø   |      | 615 |

| Thr  | Phe  | Phe  | Met   | Ala   | Phe   | Leu  | Phe   | Asn  | Trp   | Ile  | Gly   | Phe   | Phe   | Leu   | Ser   |      |
|------|------|------|-------|-------|-------|------|-------|------|-------|------|-------|-------|-------|-------|-------|------|
|      |      |      |       | 125   |       |      |       |      | 130   |      |       | ٠     |       | 135   |       |      |
| ttt  | tgc  | ctg  | acc   | act   | tca   | gct  | gca   | gga  | agg   | tat  | ggg   | gcc   | att   | tca   | gga   | 663  |
| Phe  | Cys  | Leu  | Thr   | Thr   | Ser   | Ala  | Ala   | Gly  | Arg   | Tyr  | Gly   | Ala   | Ile   | Ser   | Gly   |      |
|      |      |      | 140   |       |       |      |       | 145  |       |      |       |       | 150   |       |       |      |
| ttt  | ggt  | ctc  | tct   | cta   | att   | aaa  | tgg   | atc  | ctg   | att  | gtc   | agg   | ttt   | tcc   | acc   | 711  |
| Phe  | Gly  | Leu  | Ser   | Leu   | Ile   | Lys  | Trp   | Ile  | Leu   | Ile  | Val   | Arg   | Phe   | Ser   | Thr   |      |
|      |      | 155  |       |       |       |      | 160   |      |       |      |       | 165   |       |       |       |      |
| tat  | ttc  | cct  | gga   | tat   | ttt   | gat  | ggt   | cag  | tac   | tgg  | ctc   | tgg   | tgg   | gtg   | ttc   | 759  |
| Tyr  | Phe  | Pro  | Gly   | Tyr   | Phe   | Asp  | Gly   | Gln  | Tyr   | Trp  | Leu   | Trp   | Trp   | Val   | Phe   |      |
|      | 170  |      |       |       |       | 175  |       |      |       |      | 180   |       |       |       |       |      |
| ctt  | gtt  | tta  | ggc   | ttt   | ctc   | ctg  | ttt   | ctc  | aga   | gga  | ttt   | atc   | aat   | tat   | gca   | 807  |
| Leu  | Val  | Leu  | Gly   | Phe   | Leu   | Leu  | Phe   | Leu  | Arg   | Gly  | Phe   | Ile   | Asn   | Tyr   | Ala   |      |
| 185  |      |      |       |       | 190   |      |       |      |       | 195  |       |       |       |       | 200   |      |
| aaa  | gtt  | cgg  | aag   | atg   | cca   | gaa  | act   | ttc  | tca   | aat  | ctc   | ccc   | agg   | acc   | aga   | 855  |
| Lys  | Val  | Arg  | Lys   | Met   | Pro   | Glu  | Thr   | Phe  | Ser   | Asn  | Leu   | Pro   | Arg   | Thr   | Arg   |      |
|      |      |      |       | 205   |       |      |       |      | 210   |      |       |       |       | 215   |       |      |
| gtt  | ctc  | ttt  | att   | tat   | taaa  | gatg | gtt t | tctg | gcaa  | a gg | gcctt | cct   | g cat | ttat  | gaa   | 910  |
| Val  | Leu  | Phe  | Ile   | Tyr   |       |      |       |      | ,     |      |       |       | ٠     |       |       |      |
|      |      |      | 220   |       |       |      | ,     |      |       |      |       |       |       |       |       |      |
| ttct | ctct | ca a | ıgaag | gcaag | ga ga | acac | ctgo  | age  | gaagt | gaa  | tcaa  | igate | gca g | gaaca | cagag | 970  |
| gaat | aato | ac c | tgct  | ttaa  | ia aa | aata | aagt  | act  | gttg  | gaaa | ag    |       |       |       |       | 1012 |
|      |      |      |       |       |       |      |       |      |       |      |       |       |       |       |       |      |